BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 33.] 1936. [No. 3.

SLEEPING SICKNESS.

LESTER (H. M. O.). **Report of the Tsetse Investigation.**—*Nigeria Rep. Med. & Health Services for Year 1934.* Appendix B. pp. 69–88.

In order to provide more funds for sleeping sickness work in the field and for the equipment of sleeping sickness dispensaries, there has been a curtailment of the research side of the work, and the posts of Senior Sleeping Sickness Officer and Assistant Veterinary Pathologist have been abolished. Although Gadau is an excellent site for a research station, its inaccessibility has made co-ordination of the various field activities and co-operation with the administration increasingly difficult. For these reasons the head office was moved to Kaduna. In future the European Staff of the investigation is to consist of the Deputy Director at Kaduna, the Sleeping Sickness Officer, the Entomologist, and the Technical Assistant at Gadau, and six Sleeping Sickness Medical Officers in the field.

Research Work.—A series of new chemical compounds were supplied by the Bayer firm for examination of trypanocidal properties. The experiments started in 1933 with Surfen C and Sdt.386B and have been continued. In addition observations have been made with preparations 6210 and 6558, which are of a character similar to Surfen C and contain no heavy metal, and with preparations 5547, 6690 and 7217, which are compounds of arsenic and antimony.

Surfen C is unlikely to be of much value in the treatment of man, owing to its destructive action on the kidneys. In mice the drug was effective against *T. brucei* and *T. congolense* and strains isolated from man. With sheep infected with strains of *T. vivax* and *T. congolense* a dose of 10 mgm. per kilo proved to be more effective than a standard dose of tartar emetic, but three doses of Surfen C given at weekly intervals did not prevent relapse. Preliminary experiments on cattle infected with *T. vivax* and *T. congolense* having proved hopeful, it was decided to extend the work and to compare the action of one intramuscular injection of Surfen C with that of three injections given at weekly intervals, and with a course of 3 weekly injections of tartar emetic on groups of cattle infected with pure *T. vivax*, *T. congolense*, and a mixed infection of these trypanosomes. Some 30 animals were allocated to each experiment. Of these, 6 were given 3 weekly doses of Surfen C (10 mgm. per kilo.), 12 were given single doses of the drug, 6 were given the routine course of tartar emetic (0·06 to 0·08 cc. of a 4 per cent. solution per kilo. of body weight), and 6 were left untreated

as controls. Details of the experiments, which were unfortunately somewhat complicated by an outbreak of rinderpest, are given in a table. From the point of view of a definite cure, the results were not good, as the majority of animals relapsed within a few weeks. These findings differ from those of Hornby in Tanganyika, who reports that the majority of *T. congolense* cattle, which he treated with one dose of Surfen C, did not relapse. Although the three doses of Surfen C failed to sterilize the infection, it is to be noted that 100 per cent. of the animals were alive after six months, whereas only 6·2 per cent. of the controls survived for the same period.

The action of Sdt.386 B in mice infected with *T. brucei* was much the same as that of Surfen C. It was fairly active against strains isolated from man, but not good against *T. congolense* in mice. Some preliminary tests have been carried out on man. The initial dose was 0·1 gm. and this was followed by 0·15 gm., 2 grams, 25 gm., and 0·3 gm. at weekly intervals up to a total of 1·75 gm. [So given in the text, probably misprints for 0·15, 0·2, 0·25, and 0·3 gm.] With 4 late cases the results were not good ; the patients continued to go downhill and a treatment of tryparsamide had to be instituted. The earlier cases reacted better, and brief notes are given of 11 such cases. Although the drug was active in these cases, it was not so effective as a course of Bayer 205 would have been.

The other preparations from the Bayer Company referred to above were tested on mice infected with various trypanosomes.

Compound S. 107.—This substance was sent to the author by the reviewer, who had selected it from a large number of arsenical compounds prepared by Professor Morgan under the auspices of the Chemotherapy Committee of the Medical Research Council. The drug was tested on eight cases of sleeping sickness ; an initial dose of 1 gm. and subsequent doses of 2 gm. were given at 5 or 7 day intervals, until 25 to 30 gm. had been administered. The stimulant action was very pronounced and led to the difficulty commonly met with in experimental work with tryparsamide. The patients felt so much better that they became tired of the prolonged treatment and absconded before they had completed the course of injections. In every case patients showed very rapid clinical improvement and thought themselves completely cured after they had received 5 or 6 injections. In one case trypanosomes could still be detected in the blood after the 9th injection, but disappeared later, and in two cases trypanosomes persisted after the 6th but disappeared by the 9th injection. In two cases which completed the full course of treatment, the cerebrospinal fluid cell count fell from 332 to 1 and from 238 to 39, respectively ; in the third there was an increased cell count at the time of the final examination. Taken as a whole, the results were definitely promising. No late cases were included in the series, but it is noteworthy that one very advanced case, which had failed to react to full courses of tryparsamide, of Bayer 205, and of Antrypol, for some reason or another improved markedly on being given a course of this new drug. At the suggestion of the reviewer, who had found that S.107 was less toxic than tryparsamide, these observations are being extended and the patients are being given initial doses of 1·5 gm. and subsequent doses of 3 gm.

An experiment to ascertain the effect of exposing " premunised " animals to fresh infections did not give very hopeful results, as, up to the time of writing, *viz.* two months after the first exposure to *G. morsitans*, 6 of the 9 " premunised " cattle have died.

During the last three years various strains isolated from man and originally sensitive to tryparsamide have been maintained in guinea-pigs which have been given increasing doses of this drug. Although many hundreds of injections have been given, the strains are not yet completely insensitive to a dose of 4 gm. of tryparsamide per kilo. Lester writes that the fact that it is so difficult to induce an artificial drug-resistance in strains maintained in guineapigs shows that the natural resistance of the host must be an important factor in the production of this artificial resistance. There is, as yet, no experimental proof that repeated ineffective treatment of a human case of sleeping sickness with tryparsamide can make the strain resistant to that drug. We know that resistant strains are comparatively common, but as such strains have been isolated from untreated cases, in districts where no sleeping sickness work has been done previously, it is certain that in many cases this resistance to drugs must be a natural characteristic of the strain. The question whether ineffective treatment in man can make trypanosomes increasingly drug-resistant is an important one and the point is now being investigated.

Experiments on fly transmission showed that it was noticeably easier to pass a strain isolated from man through *G. tachinoides* than through *G. submorsitans*. In dissections made in the field infections in *G. palpalis* are usually found to be very scanty, whereas in *G. tachinoides* an infection rate of 20 per cent. is common at a certain time of the year. Similarly, under laboratory conditions it seems easier to transmit human strains through *G. tachinoides* than through *G. palpalis*. This appears to be an important point, and possibly accounts for the divergent views of workers in East and West Africa on the question of non-transmissible strains.

From the Report of the Entomologist, it appears that for nearly two years frequent censuses of the tsetse population have taken place along a track of 3½ miles in length ; this track passes through different types of tsetse bush. At the beginning of the rains the population of *G. submorsitans* starts to increase and reaches its maximum by the end of the wet season. Soon after the dry season begins, the population starts to decrease, and from December to April it is at its lowest. These facts in the main also hold good for *G. tachinoides*, and furnish a further argument for making anti-tsetse clearings early in the dry season. Not only do they then produce more lasting damage to the vegetation, but they strike at the fly community when it is entering upon an unfavourable season.

Other entomological work includes an experiment on the longevity of tsetse. This is tending to show that the patches of riverine forest are not such perfect dry sanctuaries as had been surmised, but that the fly just manage to survive the climate of the dry season in sufficient numbers to continue the species.

The remainder of the Report is concerned with the Sleeping Sickness Service. During the year 43,017 cases of sleeping sickness have been diagnosed by the Tsetse Investigation staff. Of these less than 600 cases have been treated previously. Altogether 47,187 cases have been treated during the year. Throughout the period six fully equipped teams have been at work in the field, each consisting of one medical officer, 2 African nurses, and 18 to 24 trained African dispensary attendants.

The great majority of the cases have been treated with a course of 20 to 25 gm. of tryparsamide. Adult patients have been given an

initial dose of 1 gm., followed by 2 gm. doses at 5-day intervals. It has been found that in the field it is not safe to give larger doses than 2 gm., nor to make the period between 2 injections less than 5 days. The occurrence of ocular symptoms was much more common when attempts were made to intensify the treatment. Portable stills were supplied to each team and distilled water was used for practically all injections. This was found to be a great improvement. In the past, patients complained of a variety of mild toxic symptoms, particularly after the second injection. It had been noticed that this was a very local occurrence; in some areas nearly all the patients complained of malaise, headache and fever. In rare instances there was actual diarrhoea and vomiting. Such symptoms only occurred when boiled and filtered water was used instead of distilled water.

Antrypol, a British made substitute for Bayer 205, was available towards the end of the year. Patients are at present being given 3 doses each of 1 gm. of Antrypol, followed by a course of 9 to 11 gm. of tryparsamide; with both drugs the interval between injections is 5 days.

An account of the work of the six sleeping sickness teams is then given and their observations are summarized in a table. *W. Yorke.*

GILL (C. W. Hope). **The Problem of** *T. gambiense* **Sleeping Sickness in Southern Nigeria.**—*West African Med. Jl.* 1935. Jan. Vol. 8. No. 3. pp. 10–15. [11 refs.]

In this lecture the author gives a general account of sleeping sickness. It contains nothing new. *W. Y.*

NIGERIA, COLONY AND PROTECTORATE OF: ANNUAL REPORT OF THE VETERINARY DEPARTMENT 1934 [HENDERSON (W. W.), Chief Veterinary Officer]. [**Trypanosomiasis** pp. 11–13.]

Trypanosomiasis in Nigerian cattle is widespread and causes serious economic losses. In the great majority of cases it assumes a chronic form, and when living conditions are favourable it frequently produces no apparent ill effects, but when conditions are unfavourable—shortage of food, cold and wet weather—it frequently causes death.

The only practicable method of dealing with the problem is the curative treatment of sick animals. During the year 14,000 cattle have been treated with 3 or 4 intravenous injections of a 4 per cent. solution of tartar emetic every 5 or 7 days [dose not stated]. The results on the whole have been good and the treatment is popular with the owners. Brief details are given of 275 cattle treated in this way; 17 (6 per cent.) died during treatment or within 3 months thereafter. It is stated that without treatment the death rate may be as high as 50 per cent., and in addition there is economic loss from general ill-condition.

A summary of the result of treatment by this method at the immunization camp at Zaria is given by the Deputy Chief Veterinary Officer, Mr. Griffiths. During the past four years 10,854 cattle have been treated, and provided the animals were not too emaciated and weakened there was almost invariably an improvement. The actual deaths while under treatment amounted to 2·8 per cent., but this mortality is among animals able to travel into camp from a distance; among animals treated by itinerant inoculation in the bush the mortality may be as

much as 10 per cent. or even higher. The general opinion among officers of the veterinary department is that, provided the antimony tartrate treatment is carried out before the disease has progressed to the stage when the animals are weak and emaciated, the results are good. It is also stressed that the treatment is extremely cheap and this is, of course, a very important matter.

The drug is also used as a prophylactic for trade cattle travelling by road, in order to reduce the losses which often occur during the journey. These injections have become popular with cattle traders. Experimental work is being carried out in collaboration with the Director of Tsetse Investigation on the curative value of a Bayer product known as Surfen C. *W. Y.*

MACLEAN (G.). Die Bekämpfung der Rhodesiense-Form der Schlafkrankheit in Tanganyika. [**The Fight against Rhodesian Sleeping Sickness in Tanganyika.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Sept. Vol. 39. No. 9. pp. 381–389. With 1 fig.

This paper gives a general account of the measures which are being adopted in Tanganyika to combat sleeping sickness.

The two tsetse concerned in the spread of *rhodesiense* sleeping sickness in Tanganyika are *G. morsitans* and *G. swynnertoni*, although it is possible that *G. pallidipes* may play a small part. How *T. rhodesiense* was introduced into Tanganyika is unknown. Possibly it was brought in by travellers or soldiers infected in Nyasaland, Portuguese East Africa or Rhodesia ; possibly *T. gambiense* from the Congo, Uganda or various foci in Tanganyika itself had become modified by change of insect vector into *T. rhodesiense* ; possibly it originated from *T. brucei* of game ; or possibly the original inhabitants of the country were able to harbour the parasite with little evidence of disease.

However the disease was introduced, there can be no doubt that an important factor in the production of the epidemics of *rhodesiense* sleeping sickness has been the dispersal of the natives about the country and their consequent more intimate contact with tsetse.

In order to combat the disease it is necessary either to attack the virus by treating the sick, or to break the contact between man and the fly. In practice it is extremely difficult to achieve success by one of the measures alone, the best results are obtained from a combination of both lines of attack. The methods of treatment employed in Tanganyika are :—

(*a*) *Early cases.*—Bayer 205, 1 gm. weekly for 4 weeks ; or Bayer 205, 1 gm. on the 1st, 3rd, 5th and 8th days, and 1·5 gm. on the 15th, 22nd and 29th days.

(*b*) *Advanced cases.*—After a series of injections of Bayer 205, a course of 12 weekly injections of 2 or 3 gm. of tryparsamide.

In a country of more than 450,000 square kilometres covered with tsetse bush, and in which the population is rarely more than 10, and often only 1 or 2 persons per sq. kilometre, it is obviously impossible to search out all the sick and treat them. Obviously it is first necessary to bring the people together into closer settlements, and this has the great advantage of increasing the areas under cultivation and so lessening the contact between man and fly.

In 1922, during the epidemic in Maswa, no Bayer 205 was available, but fortunately there existed in the neighbourhood a wide stretch of

open land in which the people could be settled. In Ukonongo, however, there existed no such free land, so an especially fertile region was selected in the bush and the natives caused to farm it, thereby producing a centre in which the treated sick could earn their living and at the same time lessen contact between man and the fly. There was the possibility that the aggregation of so many sick might lead to a spread of the disease, but it was hoped that this could be prevented by the use of Bayer 205. Nyonga was chosen for the first experiment of this kind. At the middle of 1925 Nyonga was inhabited by only two or three families, and apart from the small clearings made by these people there was nothing but fly-infested bush. The settlement commenced in August, 1925, and the subsequent history is shown in the following table :—

Year	Area of cultivation sq. kilometres	Inhabitants	Infected with *T. rhodesiense*
			Per mille
1925	8	1,400	28·0
1926	23	2,326	9·45
1927	27	3,000–4,660*	4·30–6·67
1933	65	3,222	4·0

*Census inaccurate.

Details are given of other similar schemes. *W. Y.*

UGANDA PROTECTORATE ANNUAL REPORT OF THE VETERINARY DEPARTMENT FOR YEAR ENDED 31ST DECEMBER, 1934 [POULTON (W. F.), Director]. pp. 9–11.—*Glossina* **Investigation and Reclamation.**

The *G. morsitans* reclamation work in South Ankole during 1934 was directed towards the control of grass fires and general observations on " fly " density. The unusual dryness of the year made it apparent as early as April that great difficulty was going to be met with in protecting the South Ankole clearings from unauthorized burning of grass and from premature firing. Some of these difficulties are described.

The various acacias and *Euphorbia candelabra*, and also the rhus and grewia thickets, showed to an increasing extent the cumulative effect of controlled annual burnings, and the great majority of the uncut areas have become far more open than they were three years ago ; there is, moreover, a strong impression that in certain areas the grass growth and grazings have improved.

In uncut areas there is a continued decrease in fly catches, and in the clearings the fly has entirely disappeared apart from an occasional straggler. The concentration of *G. morsitans* in the North Kabiganda, referred to in the 1933 report, suffered rather more disturbance in 1934 than was anticipated, owing to increased mining activity, and cars leaving that area were estimated to carry not less than 50 to 60 flies per journey from the untouched focus to the main road on the south, or to the track by the uncut belt of acacias there situated and from which *G. morsitans* had previously almost entirely disappeared. The position was met by " catching " in the acacias and by the construction of a grass-walled fumigation house across the car track.

Cultivation in this section is steadily increasing round the base of the hills, and sheep and goats are being kept in increasing numbers. The entire "fly" country of South Ankole presents a very different feature from that of 1930, when the population was sparse and density of thorn-bush and tsetse was very great.

It was stated in last year's Report that the country to the north of the River Ruizi appeared free from tsetse, but more recent work has shown the presence of several small foci which have probably been the cause of the fairly constant outbreaks of trypanosomiasis in cattle.

W. Y.

UGANDA PROTECTORATE ANNUAL REPORT OF THE VETERINARY DEPARTMENT FOR YEAR ENDED 31ST DECEMBER, 1934 [POULTON (W. F.), Director]. Appendix II. pp. 26–28.—**Trypanosomiasis** [METTAM (R. W. M.), Veterinary Pathologist].

In last year's report it was stated that a number of game had been inoculated with *T. congolense* and *T. brucei*; attempts made during the present year to reinfect a duiker and a waterbuck failed. This work suggests that in nature the game acquire a transient infection and thereafter resist further infection. If this be so they would, except for a short period, be non-infective for tsetse. A young oribi caught in a non-fly area was inoculated with *T. congolense*; it made a natural recovery after a transient infection. A wild pig resisted infection with this trypanosome, thus confirming similar observations made in previous years.

There is an impression that *T. congolense* in cattle on Buvuma Island is being transmitted mechanically by some of the many voracious blood sucking flies which exist in great numbers near the kraals, viz., Tabanids, Haematopota, Lyperosia and Stomoxys. The few *G. pallidipes* present can play only a subsidiary rôle; *G. palpalis* is numerous, but dissections show that very few are infected with *T. congolense*.

Experiments with *T. brucei* and *T. rhodesiense* show that both parasites are definitely pathogenic for stock for about six months after infection, but that if the animals are cared for and well fed they steadily put on weight and recover. It is, however, fallacious to regard *T. brucei* as a non-pathogenic parasite for cattle, as is believed by many workers. *T. brucei* is a serious menace to cattle in a *G. morsitans* area, and when superimposed on *T. congolense* causes a more rapid decline of health and is more fatal than *T. congolense* alone. It is stressed that it is extremely difficult, if not impossible, to diagnose *T. brucei* in the bovine without recourse to small animal inoculations; and that *T. brucei* is extremely resistant to treatment; of all the drugs tested during recent years, only Surfen C has given encouraging results. It is believed that owing to the difficulty of diagnosis the part played by *T. brucei* in bovine trypanosomiasis has not been fully recognized in the past; many cases regarded as pure *congolense* infections, especially those which have resisted antimosan or tartar emetic and have relapsed, have subsequently been found infected with *T. brucei*.

Further experiments have been made on the action of Surfen C in *T. congolense* and *T. brucei* infections. The dose (100 cc.) is divided into two parts and injected intramuscularly; there is no local or general reaction. Nineteen cattle infected with *T. congolense* were treated in this way; one was in very poor condition and died, but the rest

recovered and subinoculation tests suggest they are sterilized. Surfen C gave equally good results with two cattle infected with *T. brucei*. Prophylactic tests have given promising results. *W. Y.*

SOUTH AFRICAN MEDICAL JOURNAL. 1935. July 27. Vol. 9. No. 14. p. 474.—**Sleeping Sickness in the Bechuanaland Protectorate.**

This editorial article draws attention to the existence of a focus of human trypanosomiasis in Ngamiland on the borders of the South African Union. In Ngamiland chiefly in the Okavango and Chobe swamps a fatal disease, called by the natives Kgotsela, meaning light, intermittent slumber, has been known to exist. In 1909 Dr. MOFFAT of the Bechuanaland Medical Service investigated the disease, but his findings were inconclusive. In November, 1934, Dr. McKENZIE reinvestigated the disease in natives in the Chobe district, and succeeded in proving that it was in reality trypanosomiasis. Obviously it is of importance to the Union that the whole situation should be carefully examined. *W. Y.*

PORTUGUESE GUINEA. École de Médecine Tropicale. Rapport de la Mission Médicale à la Colonie de Guinée en 1932 [DE SEQUEIRA (Luís Artur Fontoura)]. [**School of Tropical Medicine. Report of the Medical Mission to Guinea in 1932.**]—86 pp. With 10 photos on 5 plates, 1 folding map & 46 figs., tables and graphs. Lisbon.

In his introduction the author quotes from the reports of previous investigators which indicate an amazing ignorance regarding the question whether or not sleeping sickness actually existed in Portuguese Guinea.

The author arrived at Bolama in April, 1932, and found a case of sleeping sickness on the Island almost immediately. At the end of the month he moved inland and established his laboratory at Buba ; after spending May and June examining the population of this district he shifted his laboratory to Bissau and transferred his attention to the north and east of the Colony. Later he returned to Buba with a motile laboratory in order to examine the infectivity of the three species of Glossina which exist there. At the end of November, after spending 7 months in the Colony, he returned to Lisbon accompanied by 3 cases of sleeping sickness in order to make a study of the trypanosomes with which they were infected.

The report is divided into three sections :—The first deals with human trypanosomiasis, the second with trypanosomiasis of domestic stock, and the third with Glossina and their degree of infection. Before leaving the Colony the author addressed a letter to the Governor enclosing particulars of 18 cases of sleeping sickness which he had discovered in various parts of the Colony. The general conclusion reached regarding human trypanosomiasis in Portuguese Guinea is that it is mildly endemic and is distributed irregularly throughout the Colony. The journeyings of the author and the distribution of human trypanosomiasis and the various species of Glossina (*palpalis*, *longipalpis*, *submorsitans* and *fusca*) are indicated in a map.

The first portion of the report consists of a lengthy clinical account of the disease as found in Portuguese Guinea, and this is followed by an equally long account of the trypanosome itself ; it contains nothing new. In the second portion of the report the author remarks that he

has examined only animals which looked ill. Of these 28 per cent. proved to be infected. The usual three parasites were found, *viz.*, *T. vivax*, *T. congolense* and *T. brucei*; a lengthy account of the morphology and pathogenicity of each is given, but here again there is nothing new. The third section contains a table showing the number of *G. longipalpis*, *G. palpalis* and *G. submorsitans* dissected and the percentage of each found infected with the various trypanosomes.

W. Y.

ZUMPT (F.). Das Glossinenmaterial der deutschen Museen, ein Beitrag zur Verbreitung der Tsetsefliegen. [**The *Glossina* Material in German Museums: a Contribution to Knowledge of the Distribution of the Tsetse-Flies.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Aug. Vol. 39. No. 8. pp. 328–337. With 1 fig.

Since the publication of his former paper in April, 1935 [see this *Bulletin*, Vol. 32, p. 722], the author has extended his knowledge of the genus *Glossina* by referring to the collections in a number of German museums, and the distributional details now given are derived partly thereform and partly from previously published records. *G. martinii*, which, as already stated (*loc. cit.*, p. 723), should in the present reviewer's opinion be regarded, provisionally at any rate, as a form of *G. palpalis*, was described by Zumpt from material from Bismarckburg, near the extreme southern end of Lake Tanganyika. Further examples of this form from Usumbura (at the opposite end of the Lake) and from Morogoro district (inland from Dar-es-Salaam) have now been identified, besides others taken in a sleeping-sickness camp at an untraceable locality called "Rumenge, Post Mdjidje." [There is grave reason to doubt the accuracy of the Morogoro record, since it is in the highest degree unlikely that any form of *G. palpalis* occurs in that region.]

To anyone familar with the great collection of tsetse-flies in the British Museum (Natural History) the present paper will be found to contain little that is new, yet one or two details may be noted. The statement that the Berlin Museum possesses *G. brevipalpis* material from the River Omo is, so far as the reviewer is aware, the first published record of the occurrence in Abyssinia of any species of *Glossina*. Confirmation in this case is needed, as also in connection with the subsequent mention of the possession by the same Museum of specimens of *G. morsitans* from Massaua—an assertion which, if true, might conceivably have an important bearing on present events.

The synonymic list with which the paper concludes is compiled from well-known publications. *E. E. Austen.*

LE PORT (L. René). Les plexo-choroidites rhomboidiennes au début de la maladie du sommeil. [**Plexo-Choroiditis of the 4th Ventricle at the Beginning of Sleeping Sickness.**]—*Bull. Méd. du Katanga.* 1935. Vol. 12. No. 2. pp. 41, 43–9, 51–5.

The author describes certain changes in the choroidal plexus which appear very early in sleeping sickness and which, in his opinion, explain a number of hitherto inexplicable symptoms met with at the beginning of the disease.

These very early changes in the choroidal plexus are almost entirely confined to the 4th ventricle. Their immediate consequence is an interruption of the communications between the ventricles and the

subarachnoid space. The only real orifices by which these two cavities communicate are the foramina of Luschka, which lie between the cerebellar peduncles in the lateral angles of the 4th ventricle. These orifices are covered by the lateral choroidal plexuses of the ventricle. It is necessary also to mention the small foramen of Magendie, the permeability of which is doubtful, but which can nevertheless, when it is not reinforced by a fibrous thickening of the median plexus, serve the functions of a safety valve.

Obstruction of the foramina of Luschka results in separation of the subarachnoid space from the ventricles, where all the cerebrospinal fluid is produced, and this automatically causes a state of disequilibrium of the tension of the fluid between the two cavities. The occlusion may reach a point—fortunately very rare and transient —where all the fluid produced is retained in the ventricles.

This condition of intraventricular hypertension gives rise to a syndrome to which the author wishes to draw attention for it is responsible for a large proportion of the troubles met with during the first stages of sleeping sickness.

Occlusion of the foramina of Luschka is rarely complete ; and if it is complete it is very rarely permanent. The usual condition is one in which the obstruction is sufficient to produce a slight disequilibrium between the intraventricular pressure and that of the subarachnoid space. Lumbar puncture reveals either a slightly diminished pressure or one that is normal. But clinically intraventricular hypertension manifests itself by the following symptoms :—headache, nausea, and a certain degree of somnolence or even of indifference. Headache is the most severe of these symptoms, the nausea is due to pressure on the 4th ventricle and is independent of troubles arising from digestive disturbances, and the somnolence has nothing to do with the toxic condition seen in advanced cases of the disease. Although papillary signs are rarely met with, a few patients may complain of floaters and flickerings. This little syndrome of intraventricular hypertension is not influenced by lumbar puncture.

When the lateral plexuses are hypertrophied to an extent that they completely occlude the foramina of Luschka, the syndrome of hypertension is much more pronounced. In this case the two dominant signs are most intense headache and psychical troubles with suicidal tendency. A third sign may be indications of papillary stasis. It is interesting to note that although the syndrome increases progressively in severity, when it abates it does so suddenly.

In these cases the subarachnoid pressure is a little lowered, and that it is not more so is due probably to the fact that the intraventricular pressure forces the fluid bathing the cortical convolutions into the subarachnoid space. Lumbar puncture may relieve the patient instantaneously, because the removal of fluid may accelerate the extraventricular prolapse of the plexus blocking the foramina of Luschka or it may render effective the foramen of Magendie. If, after 24 hours, the patient's condition is not relieved, a further lumbar puncture should be made ; if the tension is lower than at the first puncture, then obviously the desired removal of the obstruction has not been accomplished, and in order to avert damage due to hypotension a quantity of physiological saline equal to the volume of fluid previously withdrawn should be injected. If, however, the pressure is normal or raised, then either the block has been insufficiently removed or possibly the cavities still contain too much fluid ; in such

cases more fluid should be withdrawn. This type of syndrome due to intraventricular hypertension is rare; the author has met with it only 11 times out of 2,000 cases.

A third type which le Port has seen on only 4 occasions is that in which the foramina of Luschka and also that of Magendie are blocked by plexus, which is firmly fixed by fibrous adhesions. In such circumstances the patient dies quickly with exaggeration of the symptoms mentioned above. Details are given concerning these 4 patients.

Discussing the general evolution of plexo-choroiditis in trypanosomiasis, the author states that it is characterized by two phases; firstly, a hypertrophic phase seen during the first stage of the disease, and secondly, a fibrous atrophic phase met with in the middle and last stages of the disease. The syndrome of intraventricular hypertension is therefore most marked in the earlier stages of the disease and tends to disappear later on It is probable, however, that the fibrous transformation of the plexus seen in the later stages of the disease plays a certain rôle in the toxicity of the cerebrospinal fluid.

In 25 autopsies le Port has found 19 cases of more or less marked plexo-choroiditis of the 4th ventricle, and 2 cases of very severe plexo-choroiditis. Among the 2,000 sleeping sickness cases seen since 1929, 361 had slight hypertension, 11 had moderate or severe hypertension which was reducible, and 4 cases had a severe irreducible hypertension.

W. Y.

SICÉ (A.) & MOREAU (P.). Quelques réactions du système extrapyramidal au cours d'une méningo-encéphalite trypanosomique. [**Some Extrapyramidal Reactions in a Case of Trypanosomal Meningo-Encephalitis.**]—*Bull. Soc. Path. Exot.* 1935. Oct. 9. Vol. 28. No. 8. pp. 722–726.

Details are given of a chronic case of trypanosomal meningo-encephalitis in a Senegal soldier, who, the history shows, must have contracted the disease at least 3 years before he came under observation. When he was sent from Algiers to Marseilles in May, 1935, the only signs of disease were tremors of the tongue and fingers, the absence of abdominal reflexes and of the ankle jerks, and a slight reaction of the cervical lymphatic glands. The blood was negative both on direct examination and also when examined by the method of triple centrifugation: there was auto-agglutination of the red cells. Gland puncture showed the presence of trypanosomes. Lumbar puncture showed a clear fluid, pressure normal, 2,000 cells per cmm., albumen 0·85 per thousand, sugar 0·50 per thousand and chlorides 6·17 per thousand; scanty trypanosomes were discovered on centrifugation.

The case had evidently progressed in the most insidious manner without affecting the general health. There was no history of fever, or emaciation; nor during the three years he had spent in Algiers, after leaving French West Africa, did he show any evidence of apathy or lassitude, or mental disturbance. *W. Y.*

DUKE (H. Lyndhurst). **On the Factors that may determine the Infectivity of a Trypanosome to Tsetse.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. July 31. Vol. 29. No. 2. pp. 203–206.

Duke comments on CORSON's recent paper recording a remarkable instance of infectivity of *T. rhodesiense* in a reedbuck for *G. morsitans*

[this *Bulletin*, 1935, Vol. 32, p. 709]. Evidence was obtained many years ago by Duke (1912) suggesting that residence in antelope (bushbuck and reedbuck) resulted in an increased infectivity of a strain to tsetse. More recent work has, however, shown that even in an antelope prolonged residence in one and the same host tends to weaken or even destroy altogether the power of a strain to infect fly. An example of this is cited [Duke, this *Bulletin*, 1933, Vol. 30, p. 769, and 1935, Vol. 32, p. 690].

In any discussion on the infectivity of trypanosomes to tsetse one should not ignore the possibility of the occurrence in the vertebrate of a cycle of development, the phases of which are definitely related to the behaviour of the trypanosome in the intermediate host. Miss ROBERTSON (1912) first drew attention to this possibility and stated that the trypanosomes in the blood of the vertebrate host vary from day to day in their infectivity to tsetse. Duke believes that the evidence which has accumulated since ROBERTSON's work is on the whole confirmatory.

Duke then passes to a consideration of CORSON's results in light of this view. CORSON concluded that the special suitability of the reedbuck's blood affords the best explanation of his phenomenal figures. Duke agrees inasmuch as the blood of antelope affords optimal conditions to the trypanosome of this species, but he does not believe that the reedbuck is peculiar in this respect. He thinks it likely the same phenomenon will be found to occur in other species of tolerant antelope.

The article concludes as follows :—

"As to whether the trypanosome has undergone a selective change, I believe that in a tolerant species of antelope *T. rhodesiense* will manifest its maximum transmissibility : restore it to a sensitive host, *i.e.*, one that succumbs rapidly to the trypanosome, and the transmissibility will diminish either at once or after a few passages in that species of animal. But even in the antelope, after a time, transmissibility will, I believe, diminish. This is at all events clearly indicated by my own experiments. It will therefore be of interest to learn whether the animal mentioned in this paper maintains anything like the high infectivity suggested by the two tests we have been considering."

W. Y.

ROUBAUD (E.). Les modalités atypiques de l'infection trypanosomienne cyclique chez les glossines. [**Atypical Examples of Cyclical Infections of Trypanosomes in Glossina.**]—*Ann. Inst. Pasteur.* 1935. Sept. Vol. 55. No. 3. pp. 340–364. With 5 figs. [33 refs.]

This paper is concerned with an inquiry whether the three methods of cyclical development in Glossina adopted respectively by the *vivax-cazalboui*, the *congolense-dimorphon* and the *gambiense-rhodiense-brucei* groups of trypanosomes are always absolutely constant, or whether deviations from the type may occur from time to time. With this object in view Roubaud has re-examined the records made by BOUET and himself in 1910–1913 in the light of observations reported by later workers.

T. cazalboui.—After giving a detailed account of the well-known labro-hypopharyngeal method of development of this group of trypanosomes in Glossina, Roubaud draws attention to a fact which is not generally recognized, viz.—that the time when metacyclic trypanosomes appear in the hypopharynx does not coincide absolutely

with that at which the fly becomes infective. If it is true to say that only those Glossina in which the hypopharynx is invaded are capable of transmitting the infection, it is not true to say that invasion of the hypopharynx always, and immediately, renders the fly infective. This point is illustrated by reference to the report of Roubaud and Bouet, from which it appears that the flagellates require a certain time to accommodate themselves to the insect medium before they can undergo that metamorphosis which is essential for the production of metacyclic forms.

Modifications of the type of salivary infection.—Duke (1933) has recently drawn attention to instances of spontaneous disappearance of infections in Glossina: he regards it as a rare phenomenon, but Roubaud thinks that in the case of *T. cazalboui* disinfection is far from exceptional. As far back as 1908 he noticed that the infection would disappear from the labial cavity in flies kept in captivity. These researches were continued in Dahomey and showed that, as the result of age and as the result of hygrometric conditions different from those which were met with by the fly in nature, the infection of the proboscis could be considerably modified. It appears that although under good conditions the fly may remain infected during the whole of its life, the infection may disappear more or less completely in flies withdrawn from their normal environment. The most customary state met with in this partial disinfection is that in which the labial infection has disappeared completely, whilst the hypopharyngeal infection remains. Examples are given of *G. palpalis* in which only a hypopharyngeal infection was found. One fly which died 111 days after its infecting meal showed exclusively small crithidial forms in the labial cavity; the hypopharynx was sterile. This fly had, however, fed on a goat the day before the death of the animal and became infected in due course; it appears, therefore, that during its last meal the metacyclic infecting forms had been completely discharged from the hypopharynx.

Experiments are recorded which were devised with the object of ascertaining the effect of atmospheric humidity on the infectability of *G. palpalis* with *T. cazalboui*. The results indicate that keeping the flies either in a saturated atmosphere or in a dry atmosphere exercised an unfavourable influence, the proportion of flies becoming infected under these conditions being much less than of those kept under normal conditions at a humidity of about 70 per cent. Further work showed that when flies were accustomed to a dry atmosphere for a prolonged period before the infective feeds, the subsequent inhibiting effect of the dry atmosphere was much less than in unacclimatized flies.

From this work it appears that the degree of atmospheric humidity —especially dry conditions—exercises a definite influence on the type of infection: the metacyclic forms may not appear, or their development may be much retarded, the crithidia may disappear and the infection become localized for a short time in the hypopharynx, presaging a final extinction of the infection.

Similar observations on the loss of infection of the proboscis under unfavourable external conditions were made by Bouet and Roubaud (1911) on *G. morsitans* in the northern part of Dahomey and in Nigerian Sudan during the dry season. Immediately after capture 40 per cent. of *G. morsitans* were found to be infected with *T. cazalboui*; whilst, after keeping in captivity for 20 to 30 days, only 2 of 13 flies were

found infected. Other similar examples are cited. It was noticed that the hygrophilic species, *G. palpalis*, *G. tachinoides* and *G. longipalpis*, were undoubtedly more affected by desiccation of the atmosphere than the more xerophilic species such as *G. morsitans*.

TAYLOR showed that the evolution of *T. gambiense* in *G. tachinoides* was greatly influenced in a favourable direction by high temperatures. Roubaud records an observation made by him in Dahomey in 1910. In this case no evidence was forthcoming that high temperatures assisted the development of *T. cazalboui* in *G. palpalis*.

DUKE (1921) advanced the hypothesis that the kind of blood ingested by Glossina influenced the capacity of trypanosomes (*T. gambiense*) to develop in them; flies nourished on reptilian blood, after the preliminary infecting meal, exhibited a smaller proportion of infections than did those fed on monkeys. Roubaud (1910) nourished *G. palpalis*, which had had an infecting meal on goats infected with *T. cazalboui*, on birds and on reptiles, but did not observe any unfavourable effect on the development of the trypanosomes.

Roubaud gives reasons to believe that infections limited to the hypopharynx really represent the terminal stage of an infection which is on the way to extinction.

T. dimorphon-congolense.—After describing the typical mode of development of this group of flagellates in Glossina, Roubaud asks whether modifications are ever encountered. He records that he found a *G. longipalpis* in Dahomey with an infection of *T. dimorphon* entirely limited to the proboscis. LLOYD and JOHNSON (1923–24) observed progressive disinfection of the digestive tube of Glossina in immature infections of *T. congolense*. It seems that this infection once established in the proboscis persists during the life of the fly. The digestive infection may disappear, leaving the salivary infection intact, as Roubaud himself has shown when the flies are nourished on animals treated with arsenicals. DUKE (1913) has observed the same thing in the case of *T. brucei* and *T. gambiense*. But we have not much information that the same thing can happen under natural conditions. Roubaud observed in a *G. longipalpis* in Dahomey a complete infection of the proboscis with *T. dimorphon*; the pharynx, proventriculus and anterior intestine were completely negative, but at the termination of the midgut the remains of a culture of trypanosomes was found. This was apparently a case of advanced disinfection of the gut with an intact salivary infection. Another *G. tachinoides* showed a feeble infection of the digestive tract 47 days after the infective feed; the proboscis was completely negative. This might be an example of spontaneous regression of an anterior infection, but it is equally possible that certain flies may have a reduced infection of the gut for their whole life without ever developing an anterior infection. Miss ROBERTSON and later VAN HOOF and HENRARD have made somewhat similar observations with *T. gambiense* and other trypanosomes, suggesting that the flagellates may multiply in the gut of the fly without ever extending to the salivary tract. A progressive and total disinfection of the digestive tube, leaving intact the salivary infection, is more difficult to understand, at least in the case of flies fed under normal conditions.

In so far as the trypanosomes of man are concerned there are on record a number of cases (DUKE, 1933, VAN HOOF and HENRARD, 1934) in which the infection was exclusively salivary and the intestinal tube was completely negative. Possibly these were the result of

sterilization of the gut infection; but in the case of the *T. congolense* infection at least there is nothing against the hypothesis put forward by Roubaud in 1909 that the salivary infection established itself directly and immediately without being preceded by a gut infection. Whether the salivary infection is ever lost cannot yet be regarded as settled.

T. pecaudi.—BOUET and Roubaud have shown that the evolution of this trypanosome in Glossina is similar to that of the group *T. dimorphon-congolense.* DUKE (1921) expressed doubt on this statement, and especially regarding the site of the infection in the labial cavity and hypopharynx of Glossina. Roubaud writes that if *T. pecaudi* belongs to the same group as *T. brucei*, it is curious that it does not invade the salivary glands, which is so characteristic of the group *brucei-gambiense-rhodesiense.* LLOYD and JOHNSON (1924) have observed that the absence of flagellates in the proboscis in the development of the polymorphic group of trypanosomes has been insisted upon too strongly. The Luangwa Valley Commission (1912) recorded an instance of the heavy infection of the proboscis, as well as of the salivary glands, of a *G. morsitans* infected with *T. rhodesiense.* LLOYD and JOHNSON in 7 cases (2 of *T. gambiense* and 5 of *T. brucei*) observed trypanosomes of the proventricular type in the proboscis. In the course of Roubaud's work with BOUET, invasion of the proboscis of Glossina infected with *T. pecaudi* was noted in 4 of 4 cases in which the infection was confirmed by experimental inoculation. In 2 cases proventricular forms or crithidia were either fixed to the labrum or free in the labial cavity, whilst metacyclic forms were found in the hypopharynx. In the other 2 cases infection of the labrum was not observed; there was a total infection of the gut up to the pharynx and an infection of the hypopharynx. Roubaud believes that this state of things indicated an old infection in which that of the labial cavity had disappeared.

Invasion of the salivary glands by this trypanosome was not seen, but Roubaud considers that it may possibly occur, but only as a secondary phenomenon. An essential fact is that the forms seen in the proboscis were capable of producing infection of the vertebrate host. DUKE (1933) observed that BRUCE was unable to confirm the observation made by the reviewer and his colleagues (1912), *viz.* that forms infective for the vertebrate were present in the gut of *G. morsitans* infected with *T. rhodesiense.* BOUET and Roubaud had, however, made a similar observation in the case of *T. pecaudi.* [The section of this paper dealing with *T. pecaudi* is especially interesting as it seems to have been generally accepted for many years that *T. pecaudi* is synonymous with *T. brucei.* If what is written above is correct, then apparently *T. pecaudi* cannot be identical with *T. brucei.*] *W. Y.*

PERUZZI (Mario). Polimorfismo e trasformazioni globulari di alcuni tripanosomi africani nei loro rapporti con la patologia. [**Polymorphism of Certain African Trypanosomes in regard to their Pathology.**]—*Pathologica.* 1935. Sept. 15. Vol. 27. No. 527. pp. 577–586. With 3 text figs. & 24 figs. on 2 plates. [14 refs.] English summary.

The author states that the long, thin forms of the *brucei* group, with drawn out nucleus, compact and staining well, are the typical

forms which invade the host and maintain the species. The first manifestations of polymorphism appear with defects or anomalies of division and unequal distribution of the nuclear and kinetoplastic elements; the leishmanial, crithidial and leptomonad forms, he states, are derived from intermediate, short forms. Anomalous forms are present in abundance in inflamed areas, in serous exudates, and it is of such that phagocytosis occurs. In the author's summary he maintains that "the polymorphism of the trypanosomes of the *brucei-rhodesiense-gambiense* group appears to be a morphological expression of anomalies of the development of the strain . . ." giving rise to atypical torpid beings incapable of further multiplication and destined to destruction by phagocytosis. The globular forms arise from these anomalous forms. . . . Both these represent degenerated individuals in which the strain shows a tendency to exhaustion after rapid multiplication in the vertebrate host and it is towards these that the first indications of exudative and tissue reaction are observable. [The article contains some (not very convincing) figures.]

H. H. S.

POINDEXTER (Hildrus A.). **Further Observations on the Relation of Certain Carbohydrates to *Trypanosoma equiperdum* Metabolism.**—*Jl. Parasitology.* 1935. Aug. Vol. 21. No. 4. pp. 292–301.

As the result of previous work [this *Bulletin*, 1934, Vol. 31, p. 594], the author concluded that the fermentable carbohydrates of the blood form an essential part in trypanosome metabolism. The present paper describes *in vivo* and *in vitro* experiments devised with the object of investigating this hypothesis further.

The conclusion reached is that the fermentable carbohydrates seem to exert an important influence on the rate of multiplication, survival time, and virulence of trypanosomes. Injection of insulin, which decreases the blood sugar, likewise decreases the rate of multiplication of trypanosomes, and prolongs the life of the host. It was noted that less insulin was required to produce a shock as the course of the infection progressed; this corresponded with the decrease in the amount of available fermentable carbohydrate in the blood and to the liver damage.

W. Y.

CULBERTSON (James T.). **Trypanocidal Action of Normal Human Serum.**—*Arch. Pathology.* 1935. Nov. Vol. 20. No. 5. pp. 767–790. [111 refs.]

This article gives an excellent review of the present position of knowledge regarding the trypanocidal substance in normal human serum. All the main papers dealt with have already received notice in this *Bulletin*. At the end the author gives a summary of the chief points discussed, and this is reproduced here for the benefit of those who have not followed recent advances in knowledge of the subject.

"The normal serum of man will destroy the trypanosomes pathogenic for animals (*e.g.*, *T. brucei*, *T. equiperdum*, *T. equinum*, etc.) either in the test tube or in the body of rodents infected with these parasites. Human serum does not affect the trypanosomes pathogenic for man (*T. gambiense*, *T. rhodesiense* or *T. cruzi*), the common trypanosome of rats (*T. lewisi* or a trypanosome of newts (*T. diemyctyli*). One of the human trypanosomes, *T. rhodesiense*, is distinctive in that it becomes susceptible to the action of human serum after it has been passed successively through mice. The serum

of no other animals, excepting certain monkeys, manifests trypanocidal activity. The serum of some monkeys, however, *e.g.*, that of the baboon, destroys not only the trypanosomes pathogenic for the lower animals but, as well, those infective for man.

"The trypanocidal substance of human serum is found in the globulin fraction of the serum. It is thermolabile, being destroyed wholly when the serum is heated at 64°C. for an hour, and being reduced rapidly when the serum is let stand at room temperature. The trypanocidal substance passes readily through Berkefeld filters and with diminished intensity through collodion ultrafilters. It is removed from a serum by absorption with trypanosomes or bacteria (the typhoid bacillus; Proteus). The substance exhibits its activity independently of all the known components of alexin. The essential substance in the human serum which brings about the trypanocidal effect is antigenic, and a specific anti-trypanocidal antibody develops in rabbits repeatedly treated with an active serum.

"The trypanocidal substance probably originates in the normally functioning healthy liver. It is found in the blood serum and in serous exudates. The cerebrospinal fluid and the urine are without trypanocidal power. The substance appears in infants at a very early age and may be present at birth. It is probably elaborated within the body of the young child, since it is found neither to pass the placenta nor to occur in human milk. The trypanocidal power is enhanced in women late in the period of gestation and is maintained at a high level for some time after delivery.

"It seems unlikely that the action of the trypanocidal substance is that of an opsonin or an agglutinin, and the property is manifested wholly without the intervention of alexin. Some investigators have felt it acts essentially as a chemotherapeutic substance. Susceptible strains of trypanosomes become resistant or fast to human serum after repeated exposure to the serum in a manner comparable to that in which they become resistant or fast to drugs.

"Since human serum affects only those species of trypanosomes which are pathogenic for animals and which are noninfective for man, and is without effect on the trypanosomes which are infective for man, it is by some believed that the trypanocidal action of the serum is responsible for man's immunity to the animal pathogens. It is known, however, that strains of animal trypanosomes which have been rendered serum-fast still are noninfective for man, and that strains of human trypanosomes (*T. rhodesiense*) which become susceptible to human serum after repeated passage through animals retain their infectivity for man. Furthermore, the serum-resistant parasite *T. lewisi*, which is wide-spread among rats, is apparently unable to infect man. The serum of patients with trypanosomiasis is as active in trypanocidal power as that of normal persons. It appears, therefore, that the immunity of man to the animal trypanosomes depends on factors other than the trypanocidal activity of the serum.

"The trypanocidal activity of human serum is sharply reduced in diseases which cause extensive destruction of the parenchyma of the liver. Less conclusive evidence of alteration in the potency of the substance has been offered in other infectious diseases (*e.g.*, tuberculosis and syphilis) and in those attributable to deficiencies in accessory food factors. No significant reduction is observed in human trypanosomiasis. It seems possible, from the observations of some workers, that the carrier condition in hemophilia can be identified by the absence of the trypanocidal substance from the serum.

"It appears not unlikely that trypanosomes are but one form of infectious agent on which a single destructive entity in human serum acts. The fact that both the trypanocidal and bactericidal substances are removed from the serum by absorption with either trypanosomes or bacteria points toward a close similarity between the trypanocidal and bactericidal powers. The trypanocidal activity, however, differs from the bactericidal property and resembles the virus-neutralizing function of human serum in being limited to the serum of man and a few closely related primates and in

occurring without the presence of alexin. If further study indicates that these effects are all manifestations of a single entity of the serum or, what seems more likely, that they arise in analogous manners, support for the assumption that these "anti-substances" arise by immunization through contact with the specific antigen is difficult to maintain, since at no time in life does the average person suffer subclinical or abortive infection with trypanosomes." *W. Y.*

ROBERTSON (Andrew). **The Reticulocyte Response in Mice, Rats, Guinea-Pigs and Monkeys infected with** *Treponema duttoni, Trypanosoma gambiense* **and** *Plasmodium knowlesi.*—*Jl. Trop. Med. & Hyg.* 1935. Oct. 1. Vol. 38. No. 19. pp. 237–244. With 4 charts. [16 refs.]

The technique adopted was the usual one of mixing a drop of blood on a prepared slide covered with a dried film of brilliant cresyl blue. In each instance 1,000 red cells were observed (using a squared eye-piece) and the reticulocytes were expressed as a percentage. When spirochaetes or trypanosomes were present they were counted at the same time as the reticulocytes and the number per 1,000 red cells noted.

The author gives the following summary of his observations :—

" (1) Reticulocytes in mice at the first examination were found to vary from 2·2 to 12·7 per cent., average 5·49. The majority, however, had reticulocytes from 2 to 5 per cent.

" (2) Subjected to small daily bleedings there was a rise in the reticulocytes beginning about the third or fourth days and continuing up to from eight to fifteen days from the start of the examinations.

" (3) The average reticulocyte level in the mice over a period was between 3·5 and 4·5 per cent.

" (4) A marked reticulocyte response was observed after inoculation of the mice with *Treponema recurrentis* (*duttoni*). This began about four days after the first appearance of spirochaetes in the blood and reached its maximum four days after the maximum was attained by the organisms. The maximum reached was 36 per cent. reticulocytes.

" (5) After recovery the average reticulocyte level tended to be slightly lower, from 2 to 4 per cent., than previous to inoculation.

" (6) Older adult rats did not show a marked response to daily bleedings nor did their reticulocytes tend to show such variations from day to day as were seen in younger rats. The former averaged 2·85 per cent., while the latter was from 2 to 10 per cent. The younger adult rats had a reticulocytosis from 15 to 20 per cent., starting about the fifth day as a result of the bleeding.

" (7) Four young rats recovered from an infection with *T. cruzi* did not show a definite reticulocyte increase to [=at] the daily examinations and after being under observation for seventeen days their reticulocytes fell to and were maintained at a lower level. It is suggested that the disease had lessened the regenerating powers of the bone-marrow, as it were had produced an aplastic condition.

" (8) In guinea-pigs under conditions of daily blood examinations the reticulocytes are probably between 0 and 2 per cent.

" (9) When rats were inoculated with *T. gambiense* there was a reticulocytosis which was cut short owing to the swamping of the animal with trypanosomes. This rise in reticular cells followed the trypanosome increase after an interval of two to four days.

" (10) If drug treatment was administered (Bayer 205 : 0·01 mgm. per grm. body-weight) at the height of the trypanosome infection the reticulocytosis continued for from seven to eighteen or nineteen days and usually reached its maximum about the fourth or fifth day.

" (11) After this maximal reticulocytosis, the reticulocytes tended to return to a level comparable to that observed before infection. Later, after about sixty days from inoculation, the trypanosomes again appeared and multiplied rapidly. This terminal rise of trypanosomes was paralleled by a reticulocytosis similar to that seen in untreated rats.

" (12) With *T. lewisi* infections the reticulocytes of young adult rats showed a response which closely followed the daily curve of the number of trypanosomes without the delay seen in *T. gambiense* infections. After the trypanosomes had disappeared finally from the blood there was a second reticulocytosis which graphically formed a plateau.

" (13) The bone-marrow from mice, rats and guineapigs with spirochaetosis and trypanosomiasis, showed a microcytic increase.

" (14) The reticulocytes in *Silenus rhesus* are probably from 0 to 2 per cent. when examined daily over a prolonged period.

" (15) With malaria (*P. knowlesi*) the reticulocytes tend to maintain a higher level. When atebrin is given in doses insufficient to cure the infection the maximal reticulocytosis may be delayed.

" (16) Malarial parasites of monkeys as a rule were found not to occur in reticulocytes.

" (17) The anaemia of experimental trypanosomiasis and spirochaetosis in mice, rats and guinea-pigs and malaria in monkeys when severe may result in the appearance of megalocytes, but the anaemia is essentially microcytic or hypochromic in character.

" (18) There was some correlation between the number of organisms, spirochaetes and trypanosomes, and the extent of the reticulocyte response.

" (19) It is suggested that the anaemia of spirochaetosis and trypanosomiasis is due to increased erythrolysis and further, as evidenced by the reaction in treated rats to the terminal rise of trypanosomes, that proof has yet to be adduced of any inhibitory effect of the organisms on the bone-marrow activity." *W. Y.*

FRENCH (M. H.). **Nitrogen and Mineral Metabolism in** *T. congolense* **Disease.**—*Tanganyika Territory Ann. Rep. Dept. Vet. Sci. & Animal Husbandry 1934.* Part V.—Research. pp. 59–64.

From the work described in this article it was concluded that infection with *T. congolense* results in an increased rate of excretion of nitrogen, calcium, potassium and phosphates. Magnesium balances are apparently not disturbed. The effect on sodium and chlorine metabolism appears to be dependent upon the level of intake; on an adequate consumption, retention follows, but a negative balance results on low intake. *W. Y.*

VAN DEN BRANDEN (F.). La réaction de Fulton ou "méthode au chlorure mercurique" chez les rats infectés de *Trypanosoma congolense* ou de *Trypanosoma brucei.* [**Fulton's Reaction in Rats infected with** *T. congolense* **or** *T. brucei.*]—*Ann. Soc. Belge de Méd. Trop.* 1935. Sept. 30. Vol. 15. No. 3. pp. 397–398.

Fulton's reaction, or the mercuric chloride test, was employed by HORGAN, BENNET and KERNY (1929) in the diagnosis of trypanosomiasis among camels. The test consists in the addition of a drop of the serum of the suspected animal to solutions of mercuric chloride varying in strength from 1 : 10,000 to 1 : 100,000. The authors concluded that the serum of healthy animals is precipitated by the stronger solutions only, 1 : 10,000 to 1 : 20,000. Precipitation with intermediate strengths, 1 : 40,000 to 1 : 60,000, indicates that the case is probably one of trypanosomiasis, whilst precipitation with the weakest solutions, 1 : 80,000 and 1 : 100,000, warrants a positive diagnosis.

As the work of later investigators had cast some doubt on the specificity of the reaction van den Branden decided to examine the test with the serum of normal rats and of rats infected with *T. congolense* or *T. brucei*. In his earlier experiments he employed solutions of mercuric chloride of the strengths mentioned above. These, however, proved to be useless, as with only the strongest solution (1 : 10,000) was a precipitation observed. With this solution 4 per cent. of the normal sera gave positive results, 30 per cent. of the sera from *T. congolense* rats, and 33 per cent. of the *T. brucei* rats.

In later experiments he employed concentrations of mercuric chloride varying from 1 : 1,000 to 1 : 32,000. His results were :—

Of the normal sera 100 per cent. gave positive results with a concentration of 1 : 8,000 ; of the infected rats 100 per cent. gave positive results with a concentration of 1 : 16,000.

The conclusion reached is that Fulton's reaction is not sufficiently specific to be of value in the diagnosis of *T. congolense* and *T. brucei* infections of rats. *W. Y.*

VAN SACEGHEM (René). Sur le diagnostic des infections dues à "Trypanosoma vivax" chez les bovidés. [**The Diagnosis of *T. vivax* Infections in Cattle.**]—*Bull. Agric. Congo Belge.* 1935. Mar. Vol. 26. No. 1. pp. 152–154. With 1 fig.

The author states that the best way to discover *T. vivax* in infected cattle is by gland puncture : the gland juice is often positive when the blood is negative. *W. Y.*

SCHLOSSBERGER (H.) & GRILLO (J.). Experimentelle Untersuchungen ueber Misch- und Sekundärinfektion. VI. Mitteilung : Weitere Versuche ueber den Einfluss einer Mischinfektion mit Rekurrensspirochäten auf die trypanozide Wirkung des Germanins. [**Further Experiments on the Influence of a Mixed Infection with Relapsing Fever Spirochaetes on the Trypanocidal Action of Germanin.**]—*Zent. f. Bakt.* I. Abt. Orig. 1935. Nov. 15. Vol. 135. No. 4/5. pp. 203–215.

After contrasting the course of mixed infections of *T. rhodesiense* and various spirochaetes in mice with that of the trypanosome infection alone, the authors compared the effect of germanin on such mixed infections with its action on the pure trypanosome infection.

A series of mice were infected at the same time with *T. rhodesiense* and one of the following spirochaetes—*Sp. hispanica*, *Sp. obermeieri*, *Sp. duttoni*, *Sp. novyi*, *Sp. usbekistanica*, *Sp. crocidurae*, *Sp. turicata A*, and *Sp. turicata B*. The course of such mixed infections is shown in a table, from which it is seen that the *Sp. turicata A* and *B* did not influence the *rhodesiense* infection, but that the other spirochaetal strains to a varying degree exerted an inhibitory action on the trypanosomal infection ; sometimes this action was quite pronounced, whilst in other cases it was very slight. The authors came to the conclusion that the effect on the trypanosomes depended less on the particular spirochaetal strain employed than on the clinical course of the relapsing fever. The best action was observed in those individuals in which the attacks were short and the intervals long.

Whilst $\frac{1}{10000}$ gm. of germanin per 20 gm. is a certainly curative dose in simple nagana infections of mice, in mixed infections of nagana and *Sp. hispanica* such a dose will only cure if it is given in the first

3 days. If, however, the drug is given on the first day of a mixed infection definitely smaller doses are curative, *e.g.* $\frac{1}{20000}$ gm. and $\frac{1}{40000}$ gm. and even less.

The authors record experiments which confirm the observations of v. JANCSÓ [this *Bulletin*, 1935, Vol. 32, p. 702] that blockade of the reticulo-endothelium lessens the therapeutic action of germanin. According to HASSKÓ the smaller curative action of germanin in mixed infections is due to the injury to the reticulo-endothelial system caused by the spirochaetes. The increase in the action of the drug at the commencement of mixed infections is probably the result of a two-fold action. Firstly, the greater portion of the trypanosomes are killed by the chemotherapeutic action of the drug and the capacity of the remainder to multiply is inhibited ; secondly, after a relapsing fever crisis, there is hyper-regeneration of reticulo-endothelium and a consequent increase in the power of the host to deal with the trypanosomes which remain. *W. Y.*

GRILLO (Joaquin) & SCHMITZ (Joachim). Chemotherapeutische Versuche bei mischinfektionen mit zwei Trypanosomenarten. [**Chemotherapeutic Experiments on Mixed Trypanosome Infections.**] —*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. July 29. Vol. 85. No. 3/4. pp. 203–217. [18 refs.]

Experiments here described were undertaken in order to ascertain whether the infection of rats and mice with two different species of trypanosomes in any way modified the response of the parasites to various drugs.

The double infection of rats with *T. lewisi* and *T. brucei* did not result in any obvious reciprocal influence on the infections ; each developed in the usual way after the usual incubation period. The natural resistance of *T. lewisi* to germanin was in no way influenced by the presence of the nagana infection, nor was the sensitiveness of *T. lewisi* to the arseno-antimony-benzole derivative Sdt 355 increased.

Mixed infections of white mice with *T. brucei* and *T. equiperdum* ran the usual course of single infections, and the two parasites exerted no reciprocal effect on one another.

A strain of *T. brucei* rendered blepharoplastless by exposure to repeated small doses of acriflavine exhibited a definite resistance to acriflavine, but the usual sensitiveness to germanin. The dose of germanin required to cure mice with a double infection of *T. brucei* and *T. equiperdum* was the same as that necessary to cure single infections with either of these trypanosomes. *W. Y.*

BARLOVATZ (A.). La réaction méningée atoxylique. [**The Atoxylic Meningeal Reaction.**]—*Bull. Soc. Path. Exot.* 1935. Nov. 13. Vol. 28. No. 9. pp. 823–826.

In the course of his work on sleeping sickness Barlovatz has studied the rapid reaction seen in changed cerebrospinal fluids (especially the protein content) immediately after the first injection of the drug in previously untreated patients. The author is in the present paper concerned with this initial change alone. The vast majority of his observations have been made after a dose of one of the following four drugs :—

Tryparsamide (tryponarsyl) 2–3 gm., Atoxyl (trypoxyl) 0·6–1 gm., Bayer 205 (moranyl) 0·8–1 gm., Tartar emetic 0·08–0·1 gm.

Sometimes these doses were repeated after an interval of a couple of days. Lumbar puncture was made on the day of injection and at latest a week afterwards.

The immediate results produced by an injection of the various drugs is summarized in the following table :—

	Leucocytosis	Albumen content
Tryparsamide (intravenous) ...	sudden fall	slow fall
Atoxyl (subcutaneous) ...	rise or plateau	rise
Bayer 205 (intravenous) ...	slight fall	plateau
Tartar-emetic (intravenous) ...	slight fall	plateau

Tryparsamide is thus followed by a rapid fall in the number of leucocytes in the spinal fluid ; within a few days the figure may reach one-third or less. During the following weeks there is the usual increase, but it is less formidable. The albumen content is much more stable than the leucocytosis and responds more slowly. It reacts, however, to atoxyl by a sudden and massive increase, which is the chief characteristic of the atoxylic meningeal reaction. The leucocytes usually show at first a moderate increase, but they may also rise rapidly.

The above is the general rule, but actually variations occur. The meningeal reaction may follow tryparsamide, but this is quite exceptional and happens in less than 1 per cent. of cases ; and it occurs in only about 5 per cent. of cases treated with germanin or tartar emetic. With atoxyl the reaction is sometimes very slight and it may fail altogether, but with this drug it is the rule rather than the exception.

Details are given in tabular form of 4 patients treated with atoxyl :—

Names	No. of days between the two examinations	Leucocytes		Albumen	
		Before	After	Before	After
Kasambula	(lumbar puncture) 7	150	165	0·40	0·48
	(occipital puncture) 6	130	120	0·30	0·44
Tshisupa	(lumbar puncture) 8	210	215	0·44	0·52
	(occipital puncture) 10	130	120	0·42	0·57
Mulenda	(lumbar puncture) 7	155	820	0·35	0·55
	(occipital puncture) 7	42	720	0·39	0·53
Beya	(lumbar puncture) 6	13	20	0·15	0·27

The general conclusion is that atoxyl often provokes, in the already changed spinal fluid of sleeping sickness cases, an increase of leucocytes and of albumen ; the increase is sudden and sometimes important. This meningeal reaction is not seen with the other three drugs, *viz.* tryparsamide, germanin and tartar emetic. *W. Y.*

VAN DEN BRANDEN (F.) & APPELMANS (M.). Les troubles visuels au cours du traitement de la trypanosomiase humaine par la tryparsamide (tryponarsyl, trypotan, novatoxyl). [**Visual Disturbances in the Course of Treatment of Human Trypanosomiasis by Tryparsamide.**]—*Bruxelles-Méd.* 1935. Oct. 20. Vol. 15. No. 51. pp. 1405–1421. [51 refs.]

Much of the work referred to in this paper has already been published elsewhere and summarized in this *Bulletin* [1934, Vol. 31, p. 573].

Attention is drawn to the fact that visual disturbances are met with in no less than 20 per cent. of second stage cases of human trypanosomiasis treated with tryparsamide. These accidents are serious because they involve both eyes and frequently lead to blindness as the result of bilateral optic atrophy. After considering the clinical characters of these visual troubles, the authors attempted to reproduce them in the rabbit with the object of throwing light on their pathological mechanism.

BROUARDEL and POUCHET, who have studied the poisonous effects of inorganic compounds of arsenic, have not noticed sensory disturbances. Acute poisoning produces choleriform symptoms: epigastric pain, vomiting, diarrhoea, aphonia and muscular cramps; death occurs on the third to fifth days with delirium and convulsions. Chronic poisoning develops in 4 periods: the first is characterized by digestive disturbances; the second is marked by cutaneous eruptions, erythemas, exfoliations, pigmentations, urticaria notably of the eyelids, and by laryngo-bronchial catarrh (sometimes aphonia), extending to the mucous membrane of the nose and conjunctiva. The third period is characterized by disturbances of sensation, numbness of the limbs, shooting pains; and in the fourth period palsies develop and the patient is easily fatigued. Cure is frequent, but convalescence is protracted; death, when it occurs, is due to lesions of the heart, liver and kidneys. Visual troubles following poisoning by inorganic arsenicals are very rare and quite different from the amblyopia due to aromatic arsenicals; a large dose of an inorganic arsenical may produce a central scotoma with great loss of vision and haemorrhages of the retina, but these troubles tend to disappear when the intoxication ceases.

Numerous cases of blindness have been recorded during the treatment of various diseases by pentavalent aromatic arsenicals, such as acetylarsan, stovarsol and particularly atoxyl and tryparsamide. The amaurosis produced by atoxyl is the gravest of the toxic amblyopias; when visual troubles proclaim themselves they almost always lead to blindness from optic atrophy. Visual disturbances have been frequently observed during the treatment of trypanosomiasis with tryparsamide by PEARCE, CHESTERMAN, MARUGO, LAIGRET, etc. The authors have observed them 24 times in 118 cases. Details of these cases are summarized in a table, and are discussed at some length [this *Bulletin*, *loc. cit.*]. From the clinical facts recorded in this part of the paper, the following conclusions are drawn:—

1. In poisoning by inorganic arsenicals visual troubles are rare and late. The symptoms and evolution are quite different from those observed in the course of a treatment with atoxyl or tryparsamide, and they are reversible.
2. The visual disturbances following treatment of trypanosomiasis with tryparsamide are frequent; they often occur early in the treatment and are only partially reversible.
3. These troubles occur almost exclusively in second stage cases of trypanosomiasis where the spinal fluid is changed; they are the more frequent as the spinal fluid is the more changed.

The next portion of the paper describes experiments undertaken with the object of producing optic changes in rabbits analogous to those seen in man. Van den Branden has already shown that when rabbits are given large doses (1·25 gm. per kilo.) of tryparsamide they develop renal lesions [this *Bulletin*, 1935, Vol. 32, p. 695]. So

far, however, optic atrophy has never been observed in these animals as the result of large doses of arsenicals. The authors therefore decided to attempt to reproduce experimentally in rabbits the optic lesions which are found in man. The rabbit was chosen as the experimental animal, because it is the animal which is usually used for testing arsenicals, and it lends itself readily to examination of the fundus by means of the electric ophthalmoscope. The drugs used were atoxyl and tryparsamide. Total doses varying from 60 cgm. to 8·5 gm. were given either intravenously or retrobulbarly; and not only pure, well-preserved products were used, but also old products, such as tryparsamide which has assumed a rose colour and is considered in Africa to be especially dangerous to vision.

The results of these experiments are given in a table. As they did not yield any positive result they were repeated in rabbits infected with *T. congolense*, which runs a relatively chronic course in these animals. The conclusions drawn from this work are:—

1. A single injection of tryparsamide (normal or changed) in a normal or infected rabbit does not produce optic atrophy comparable to that sometimes observed in man.
2. Repetition of weekly injections appears to be more harmful to the optic nerve. Ophthalmoscopic examination suggests that tryparsamide may produce vascular changes in the retina.
3. The changes in the fundus are more frequently seen in rabbits infected with trypanosomes than in normal rabbits.

The last portion of the paper is concerned with a discussion of the pathogenesis of the visual troubles occurring in man [this *Bulletin*, *loc. cit.*]. The general conclusion reached is that the lesions have a mixed origin. It is not denied that optic atrophy due to arsenicals occurs, and optic neuritis due to trypanosomiasis is certain; but these forms are rare. Usually the condition is seen in individuals suffering from chronic trypanosomiasis, the tryparsamide striking the final blow on an optic nerve rendered fragile by the central nervous infection.

W. Y.

COLLIER (W. A.) & KRAUSE (Magdalene). Die chemotherapeutische Wirksamkeit von Arsenverbindungen schwefelreicher Eiweissspaltprodukte. [**The Therapeutic Activity of Arsenical Compounds of Sulphen Rich Products from Proteins.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1935. July 18. Vol. 117. No. 2. pp. 190–195.

As the result of previous work the authors had reached the conclusion that probably organic components, consisting of high molecular decomposition products of keratin, rich in sulphur, would be an excellent vehicle for therapeutically active metals. A number of such compounds of arsenic were consequently prepared: these are condensation products of oxy-, amino-, and oxy-amino-phenylarsenoxides, and their substitution products with high molecular, sulphur-rich, decomposition products of keratin.

The condensation products, which were prepared in the laboratory of Johann A. Wülfing, Berlin, are bright-coloured, mainly white substances, and for the most part easily soluble in water, although some of them require the addition of sodium bicarbonate before they will form a clear solution. The arsenic content of 12 (labelled W I–W XII) of these compounds and their therapeutic indices in mice

infected with nagana are given in a table and contrasted with those of various salvarsans. It is seen that the arsenic content is relatively very low. The drugs were administered intravenously, subcutaneously and orally. Four of the compounds (W VI, W VII, W XI and W XII) showed a therapeutic index which surpassed that of neosalvarsan. The best was W VII on intravenous injection with an index of 1 : 45. On oral administration they gave good results. Rabbits in an advanced stage of the disease were cured. Certain of the compounds (W VII, W VIII, and W XI) proved superior to salvarsan in the treatment of *Sp. recurrentis* infections of white mice. *W. Y.*

HORNBY (H. E.). **On the Nature of the Resistance to Treatment shown by Some Cases of Bovine Trypanosomiasis.**—*Tanganyika Territory Ann. Rep. Dept. Vet. Sci. & Animal Husbandry 1934.* Part V.—Research. pp. 37–39.

Antimosan and tartar emetic still remain the standard remedies for infections due to *T. congolense* and *T. vivax.* All work on this subject suggests that the action of the two drugs is identical, and that if an infection is able to resist the action of one it is likewise able to resist the other. Of great importance to veterinarians are the researches of YORKE and his colleagues on drug-resistance. They showed that while it is extremely difficult, or even impossible, to produce a tartar emetic resistant strain by the ordinary direct method of administering sub-curative doses of the drug, it is extremely easy to produce a resistant strain from an atoxyl-resistant strain. They also showed that resistance to naganol (Bayer 205) does not involve resistance to antimonial compounds. It would appear, therefore, that, so long as we refrain from using arsenical drugs prior to antimonials, there is no danger of establishing antimony-resistant strains. Nevertheless, in practice some cases of trypanosomiasis seem to be incurable by antimonials, and the question arises whether this is due to idiosyncrasy of the host or wholly or in part to a treatment-resistant character of the particular strain of parasite. It was with the object of finding an answer to this question that the present work was undertaken.

Details are given of a buffalo infected with *T. congolense* which proved highly resistant to antimonials. The animal had to be destroyed as incurable on 30th January, 1933, after having received 34 injections of antimosan and tartar emetic between August, 1931 and January, 1933. A healthy animal was inoculated from this buffalo on 27th October, 1931, and this animal became infected and was cured by two courses of tartar emetic.

An ox infected with *T. congolense* was treated unsuccessfully with many courses of antimosan and tartar emetic between August, 1932 and March, 1934. At a late stage of the infection, in November, 1933, a healthy ox was inoculated with the blood of this animal, and from this two other oxen were subinoculated; both were quickly cured by antimosan or tartar emetic.

The general conclusion reached from this work is that unusual refractoriness to antimonial treatment is more often due to a host idiosyncrasy than to special resistance on the part of the parasite.

W. Y.

FRENCH (M. H.) & HORNBY (H. E.). **Studies concerning the Effect of the Plane of Nutrition on the Course of Animal Trypanosomiasis. 1.—Introduction, and 2.—*T. congolense* Disease from Infection to Crisis.**—*Tanganyika Territory Ann. Rep. Dept. Vet. Sci. & Animal Husbandry 1934.* Part V.—Research. pp. 40–58. With 11 figs.

Experiments are described from which it is concluded that the course of *T. congolense* disease from infection to crisis is uninfluenced by planes of nutrition higher than those of bare maintenance.

In their introduction, the authors point out that in tropical Africa the three trypanosomes of veterinary importance are *T. congolense*, *T. vivax* and *T. brucei*. There are quite definite differences between the diseases due to these three parasites, *e.g. T. brucei* produces a blood disease in rats and guineapigs, whereas in rabbits and goats the most pronounced lesions are in the more solid tissues ; *T. congolense*, however, is essentially a blood parasite, and the disease due to it is essentially an anaemia. As *T. congolense* is at least as important as the other two parasites, and as its behaviour within the mammalian host is better known, the authors selected it for their first experiments. The experiments have been divided into two parts ; the first dealing with the stage from infection to the crisis of impending death or commencement of recovery, and the second with the period of recovery.

Although there are neither cattle nor donkeys, and comparatively few sheep, goats and dogs within the thick tsetse belts of East Africa, owing to the fatal effect of continual infection by pathogenic trypanosomes, yet any single infection by itself is by no means necessarily fatal. In fact Hornby and BAILEY (1930) have stated the opinion that " uncomplicated disease due to a single infective dose is rarely fatal if a diet adequate to meet the calls of anaemia is provided."

Notwithstanding the fact that it is generally assumed that good feeding is essential to recovery from *T. congolense* disease, there are no precise experiments on the subject, or on the equally important question whether feeding influences the course of the disease in its earlier state. It is with the latter matter that the present paper deals. The experiments were conducted on 11 oxen of which two were uninfected controls. For details the paper itself must be consulted.

No indication was found that higher planes of nutrition exert a beneficial influence against the development of the disease. In all cases, whether good or poor rations were provided, the production of anaemia followed the same course, nor was there anything to suggest that nutrition influences the degree of infection. Better feeding did not help the formation of antibodies, since neither body temperature nor the degree of infection was influenced by nutrition. *W. Y.*

ROTHERMUNDT (M.) & RICHTER (R.). Experimentelles ueber Solu-Salvarsan. [**Experiments on Solu-Salvarsan.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Aug. 30. Vol. 85. No. 5/6. pp. 474–487.

Observations are recorded on the toxicity and therapeutic action of a new arsenobenzol derivative prepared by the I. G. Farbenindustrie under the name of solu-salvarsan.

The drug is supplied in solution ready for use, and can be given either intramuscularly or intravenously. The solution is slightly alkaline and is of such a strength that 1 cc. contains 0·02 gm. of arsenic.

The toxicity of the freshly-prepared substance and of the solution kept 30 days was tested on mice, rats and guineapigs. For mice the toxic dose was from 0·3 to 0·5 cc. and the tolerated dose was 0·25 cc. per 20 gm. of body weight; for rats the toxic dose was 5·0 to 7·0 cc. and the tolerated dose 4·0 cc. per kilo. of body weight; and for rabbits the doses on subcutaneous injection were respectively 3·0 cc. and 1·5 cc. per kilo. of body weight. Similar results were obtained with solutions kept for 30 days, no increase in toxicity being observed.

The therapeutic action of solu-salvarsan was determined in mice infected with nagana or Russian relapsing fever and in rabbits infected with syphilis. It was found that doses of 0·0125 cc. to 0·02 cc. cured nagana mice. In the relapsing fever mice 0·0125 cc. caused the disappearance of spirochaetes from the blood in 2 days and 0·025 cc. caused their disappearance within 24 hours. In experimental rabbit-syphilis the curative dose was 0·15 cc. per kilo.

From this work it appears that solu-salvarsan exhibits a strong parasiticidal action and is less toxic than other arsenobenzol derivatives. The therapeutic index of solu-salvarsan for mice infected with nagana is 1 : 20 as compared with 1 : 40 for neosalvarsan, but for mice infected with *Sp. obermeieri* the ratios are 1 : 10 for solu-salvarsan and 1 : 2 for neosalvarsan. In the case of rabbit-syphilis the drugs are equally active.

The last part of the paper records a large number of prophylactic experiments made with solu-salvarsan and neosalvarsan. Mice were given various doses of one or other of the two drugs, and then at daily intervals afterwards a certain number were inoculated with nagana. The length of protection conferred was about the same in each case and varied directly with the amount of drug given. When the dose approximated to the maximum tolerated dose the mice were protected for about 5 days. *W. Y.*

YORKE (Warrington). Contribution au côté biologique de la chimiothérapie. [**Contribution to the Biological Side of Chemotherapy.**] —*Riv. di Malariologia.* Sez. II. 1935. Vol. 14. Supp. to No. 3. pp. 53–71. With 3 graphs.

In this lecture the author summarized the recent work of his colleagues and himself. The various matters dealt with have already been noticed in this *Bulletin.* *W. Y.*

BROWNING (C. H.). **Chemotherapy—the Progress of Thirty Years and the Prospect.**—*Glasgow Med. Jl.* 1935. Nov. Vol. 124. No. 5. Chir. pp. 1–16.

This lecture gives a general review of the progress of chemotherapy during the last 30 years. It contains nothing new and must be consulted in the original by those interested. *W. Y.*

SCHILLING (Claus) with H. SCHRECK, H. NEUMANN & H. KUNERT. Versuche zur Schutzimpfung gegen Tsetsekrankheit. II. Teil. [**Experiments on Protective Inoculation against Tsetse-fly Disease.**] —*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Aug. 30. Vol. 85. No. 5/6. pp. 513–528.

The work with which this paper deals has already been published elsewhere and noticed in this *Bulletin* [1935, Vol. 32, p. 714].

W. Y.

DUKE (H. Lyndhurst). **Old "Laboratory" Strains of the Polymorphic Trypanosomes.**—*Lancet.* 1935. Sept. 21. pp. 665–667.

This paper is apparently called forth by Browning and Gulbransen's recent communication regarding a strain of *T. brucei* passaged in mice. In the early passages the infection was relatively chronic and relatively resistant to arsenicals, whilst in the later passages it was relatively virulent and the infected mice were readily cured by the same drugs. [This general fact has, of course, been known for many years by all who have interested themselves in experimental chemotherapy. For example, *T. rhodesiense* infections in man are notoriously resistant to arsenical treatment, and the reviewer and his colleagues showed some years ago that freshly isolated strains of *T. rhodesiense* and *T. brucei* in laboratory animals were highly resistant to arsenicals, whereas infections by old laboratory strains of *T. rhodesiense* were readily curable.]

Duke points out that among the changes which may occur in trypanosomes during prolonged maintenance by direct passage in laboratory rodents are: (1) loss of power to develop in tsetse; and (2) increase of virulence; a third character which may also change is pathogenicity to man.

Once a strain has lost its power to develop in tsetse it retains for the student of human trypanosomiasis an interest mainly academic. Many old laboratory strains are now in all probability unable to develop in Glossina. This subject has been ignored by most investigators, although REICHENOW [this *Bulletin*, 1935, Vol. 32, p. 34] has studied what appears to be a closely associated if not identical character, *viz.* the culturability of these organisms in artificial media. Probably TAYLOR encountered one or two non-transmissible strains in his work in Nigeria [this *Bulletin*, 1933, Vol. 30, p. 105]. In his introductory remarks TAYLOR refers to Duke's views as follows:—"If this total loss of transmissibility occurs in nature with any frequency, and Duke's analysis of East African *T. gambiense* strains suggests this, then it would seem that *T. gambiense* strains are constantly becoming extinct, a conclusion of very considerable importance from the epidemiological standpoint." Duke states that his own experience of naturally occurring non-transmissible strains has been derived entirely from *T. gambiense* regions where *G. palpalis* is the only tsetse. Even here they were exceptional; and he has met with only one non-transmissible "wild" strain of *T. brucei* and none of *T. rhodesiense* in its typical form virulent to man.

The second modification, increase of virulence, may occur in nature. It is possible that direct transmission by Glossina plays an accessory part in the spread of the *brucei* group in nature, in the form of epidemics in man or domestic animals. But this must be incidental to the normal propagation of these trypanosomes. In nature increasing virulence for a vertebrate host is actually an embarrassment to a trypanosome, and yet in the laboratory there is a tendency to regard it rather as a kind of adaptation of the parasite to its host [and undoubtedly it is]. Duke complains that an enormous amount of work has been done in European laboratories during the last 20 to 30 years with trypanosomes which have little resemblance to their ancestors fresh from human or ruminant blood.

Laboratory changes and trypanocidal drugs.—A field biologist may well look askance at the majority of the representatives of *T. gambiense*

or *T. brucei* in European laboratories. Increased virulence is a common result of prolonged maintenance of a trypanosome in rats or mice, and there is also evidence that the guineapig in course of time exerts a definite influence upon these organisms. Recently Duke has found that pathogenicity to man and transmissibility by tsetse may diminish apparently to vanishing point on maintenance of a strain in guineapigs.

It is interesting to determine how long old laboratory strains retain their power to infect man, but the interest is mainly academic, because such strains may in the meantime have lost their power to infect tsetse. For instance, a strain of *T. gambiense* isolated from man in 1920 was still infective for man on subcutaneous inoculation in 1935, but it was completely non-transmissible by tsetse.

It is easy to make an old laboratory strain of say *T. brucei* resistant to drugs, and this resistance, as has been shown by YORKE and his colleagues, is not diminished by cyclical passage through Glossina. Certain strains of *T. gambiense*, on first isolation from man possess a considerable resistance to arsenic; this may be a natural feature of the strains or the result of previous exposure to arsenicals. One attempt in Nigeria and one in Uganda to make a really sensitive strain of *T. gambiense* arsenic-resistant have resulted in a serious impairment of transmissibility. If this proves to be a general fact, then the development of drug-resistance in an ordinary arsenic-sensitive *T. gambiense* has no practical significance. [Much more work is, however, required on this important subject before we should be justified in accepting this hypothesis, which seems out of harmony with many observations.] Duke admits, however, that there is no denying the danger of producing strains resistant to arsenic by improper treatment of natives suffering from trypanosomiasis in *G. palpalis* and *G. tachinoides* areas. In practice this danger can be met by combining arsenic treatment with Bayer 205, or possibly by replacing arsenicals altogether by Bayer 205.

The author contends that the moral behind all these reflections is "to abandon the study in laboratories the world over of ancient and atypical laboratory strains of the tsetse-carried trypanosomes, and take up in their place samples recently isolated from their natural habitat. Study these until they start degenerating and then scrap them, and so build up a first-hand knowledge of the trypanosomes as they really are in nature. . . . One result will be fewer disappointments over the claims made for new trypanocidal drugs, when the time comes to test them out in real life."

[The reviewer who has had great experience during the last 8 years in examining the trypanocidal activity of new compounds is quite unable to subscribe to this doctrine. Most of those who are engaged in this work are well aware that it by no means follows that because a drug will cure laboratory animals infected with one or other of the old laboratory strains, it will necessarily cure a naturally infected human being or a domesticated animal. But we have the great advantage of knowing that if we fail to cure our laboratory animal infected with our old laboratory strain the drug is not likely to be of any use in the field. The old laboratory strains are virulent for small laboratory animals and have for the most part reached a uniform degree of sensitiveness to drugs. They are therefore very valuable as a sort of common indicator for the preliminary sorting of new potential trypanocidal substances. There are a number of weighty objections to the course recommended by Duke. To mention two

of them : Duke himself states in the present article that natural strains even of the same trypanosome vary amongst themselves in their sensitiveness to drugs at the time of isolation. As the reviewer and his colleagues have shown, some of these strains are so resistant to such well-tried drugs as tryparsamide or orsanine that they would be quite useless as indicators for testing new compounds, whilst others exhibit intermediate degrees of resistance. A second objection to the use of freshly isolated strains for this work is that such strains frequently run a chronic course in laboratory animals and are for this reason less well adapted for examination of the trypanocidal activity of new compounds. Finally, we must not forget that such well-tried trypanocidal substances as atoxyl, tryparsamide, orsanine and Bayer 205 all owe their discovery to work on old laboratory strains of trypanosomes.

If there be " disappointments over the claims made for new trypanocidal drugs," they do not result from the method of conducting the preliminary tests of new compounds on small animals infected with old laboratory strains, but from the ignorance of those who are neither able to distinguish between a mouse and a man, nor to appreciate the fact that trypanosome strains change during prolonged syringe passage through laboratory animals.] *W. Y.*

TOKURA (N.). Ueber Trypanotoxin von *Trypanosoma gambiense* und *equiperdum*. [**Trypanotoxin of** *T. gambiense* **and** *T. equiperdum*.] —Reprinted from *Igaku Kenkyu*. 1935. June. Vol. 9. No. 6. 14 pp. With 6 coloured figs. on 1 plate. [10 refs.]

A method of preparing trypanotoxin is described, and the effect of this upon the cornea of rabbits is examined.

In his introduction the author briefly reviews the earlier work on the subject of toxin formation by trypanosomes. The method used in the present work for preparing trypanotoxin was based upon Besredka's method of extracting endotoxins from bacteria. The blood of mice at the height of infection was collected in 2 per cent. sodium citrate solution and the trypanosomes were separated from the red corpuscles by fractional centrifugation. The trypanosomes were then collected in a narrow graduated centrifuge tube and centrifuged for 20 minutes at 3,000 revolutions in order to measure their volume. The deposit was then taken up in physiological saline and centrifuged in large centrifuge tubes and at high speed, and the supernatant fluid removed. To the deposit sodium chloride was added in the proportion of 0·1 gm. to each 0·2 cc. of trypanosomes and the mixture ground up with a sterile glass rod, distilled water being added drop by drop up to 100 times the amount of sodium chloride used. The final result of this was an emulsion consisting of 2 per cent. of trypanosomes in 1 per cent. of sodium chloride solution. This was divided into two parts, *viz.*—(A) which was allowed to stand for 2 hours at 37°C., and (B) which was heated at 60°C. for half an hour ; both were stored in the ice-chest for 24 hours. The emulsions were then centrifuged at high speed and the supernatant fluids (trypanotoxin) removed. Preliminary trials with these two specimens of trypanotoxin showed that the latter (*i.e.* the one heated to 60°C. for 30 mins.) was considerably the more potent, and consequently it was the one used in all the work described in this paper.

The test was performed in the following manner. Rabbits were firmly fixed and a 5 per cent. solution of cocaine dropped into the eye; the globe was then fixed with hooked forceps and 0·1 cc. of trypanotoxin—either the original solution or various dilutions thereof—injected with a very fine needle into the cornea. A circumscribed, sharply delimited, whitish, opaque, definite swelling resulted. This swelling should within a few hours be completely absorbed. In order to examine the reaction a fluorescent solution (fluorescine 0·5, sod. bicarb. 1·5, dist. water 100) should be dropped in the eye on the following day and each day afterwards for a week. If there is any ulcer of the cornea, the ulcerated region will appear more or less strongly green or yellow.

The following degrees of reaction were noted :—

1. Typical ulcer formation. Deep green to dirty yellow colour; edge more or less definitely undermined; conjunctiva hyperaemic and cornea cloudy; haemorrhage in the anterior chamber; later staphyloma formation. Healing occurs in 10 to 18 days, leaving a white area.

2. Moderate ulcer formation. Deep green to dirty yellow colour, edge slightly undermined; no staphyloma. Healing in 6 to 9 days leaving a white area.

3. Slight ulcer formation. Round sharply limited, light green colour; surface slightly rough. Heals in 2 to 5 days with hardly a trace.

The experiments are described in some detail and the results are summarized in tables. The following summary is given :—

1. *T. gambiense* and *T. equiperdum* produce a trypanotoxin which will produce circumscribed ulcers in the cornea of rabbits.

2. Trypanotoxin withstands heating to 60°C. for 30 mins., but is completely destroyed by a temperature of 80°C. for 30 mins.

3. It is also destroyed by N/5 NaOH and by N/5 HCl solutions.

4. It loses its activity when exposed to direct sunlight for 2½ hours or to ultraviolet rays for 1¼ hours.

5. It retains its potency when dried for at least 20 days.

6. The cornea of a rabbit immunized with *gambiense* or *equiperdum* formalized vaccines is less susceptible to the corresponding trypanotoxin. Similarly the reaction is modified if the rabbit is given a dose of the corresponding antitrypanosomal serum, but not if a heterologous antitrypanosomal serum is administered.

In an appendix the author remarks that he was unable to obtain any reaction in the skin of rabbits with trypanotoxin when injected in amounts varying from 0·1 to 0·25 cc. He therefore conceived the idea of examining the Shwartzman's phenomenon with trypanotoxin. Eight rabbits were prepared by an intracutaneous injection into the shaved skin of the abdomen of 0·25 cc. of *gambiense*- and *equiperdum*-trypanotoxin and of typhus toxin, each toxin being given in two places. After 24 hours 2 of the rabbits were given an injection of 2·5 cc. of *gambiense* trypanotoxin, 2 a similar injection of *equiperdum* trypanotoxin, 2 typhus toxin, and 2 normal saline. The reactions are shown in a table. The combination typhus toxin preparation + typhus toxin injection produced a definite ecchymosis in the corresponding areas, the combination typhus toxin preparation + trypanotoxin injection gave a similar but slighter ecchymosis. There was no reaction in the areas prepared with trypanotoxin. *W. Y.*

Pottier and van den Branden believe that their figures justify the conclusion reached in their previous papers, *viz.*, that 1 gm. per kilo. should be the official test dose. They consider that if the smaller dose (0·75 gm.) is selected there would be a risk of passing an abnormal lot of the drug. They do not question the accuracy of the results of LAUNOY and PRIEUR, but consider the cause of the discrepancy must be looked for in local conditions, *viz.*, the race of animals, their nutrition, climatic conditions, etc.

The authors next pass to a consideration of the toxicity of tryparsamide for the mouse. They point out that the chief danger to man is optic neuritis and that, whereas the main toxic symptoms exhibited by rabbits are disorders of the alimentary canal, mice exhibit nervous symptoms (dancing mice of Ehrlich). Possibly, therefore, information of much value might be obtained from tests of samples of the drug on mice. Various samples of tryparsamide were selected and each was injected subcutaneously into a group of 10 mice : the dose in each case was 90 mgm. per 20 gm. of mouse. The results are shown in the following table :—

	Mortality (per cent.)	Nervous signs (per cent.)
1. Glyphenarsine normal...	0	10
2. ,, ,, ...	0	20
3. ,, ,, ...	0	20
4. ,, ,, (same product)	10	40
5. Glyphenarsine spoiled in manufacture	10	60
6. Glyphenarsine made yellow by the transient action of chlorine	0	60
7. Glyphenarsine A suspect, returned after prolonged sojourn in Congo	0	100

These results suggest that possibly different specimens of tryparsamide exhibit different degrees of neurotropism, and that the mouse may be a valuable test animal. *W. Y.*

VAN DEN BRANDEN (F.), APPELMANS (M.) & POTTIER (R.). La toxicité du tryponurile sur le parenchyme rénal. [**The Toxicity of Tryponurile on the Renal Parenchyma.**]—*Ann. Soc. Belge de Méd. Trop.* 1935. June 30. Vol. 15. No. 2. pp. 225–228.

In a previous paper [this *Bulletin*, 1935, Vol. 32, p. 695] the authors have drawn attention to the renal lesions produced by tryponurile, which is a product of L'Union Chimique Belge, consisting of equal parts of tryponarsyl and urenile (hexamethylene tetramine). The present work was instituted with the object of ascertaining firstly, whether it was the tryponarsyl or the urenile, or the combination of both, which causes the damage to the kidneys; and secondly, the dose which was necessary to produce these serious lesions.

Three groups of rabbits all weighing about 2 kilos. were injected intravenously with increasing doses of tryponarsyl, urenile, and tryponurile, respectively. Eight days later the animals were killed, the kidneys fixed in 10 per cent. formalin, sections were cut in paraffin and stained with haematoxylin, eosin and safronin.

In none of the 7 rabbits which received doses of tryponarsyl, varying from 0·05 gm. to 1·25 gm. per kilo., were any renal lesions discovered. In the 5 rabbits which were given doses of urenile, varying from 0·05 gm. to 0·75 gm. per kilo., discrete lesions were found in the renal parenchyma and certain glomeruli were congested. In the 3 rabbits which received

small doses of tryponurile, *i.e.*, 0·1 gm. to 0·5 gm. per kilo., practically no lesions were found ; but in the two animals which were given larger doses, *viz.*, 1·0 gm. and 1·5 gm. of urenile per kilo., widely disseminated grave lesions were seen.

The general conclusion is that while it is not possible to say that a dose of 0·5 gm. of urenile is harmless, it is clear that a dose of 1·0 gm. per kilo. may produce very severe renal changes. In the treatment of human trypanosomiasis tryponurile should not be given in larger doses than 3 gm. to 4 gm., at any rate to commence with. *W. Y.*

BOURGUIGNON (G. C.). Note documentaire au sujet des trypanosomiases animales. [**Documentary Note on the Subject of Animal Trypanosomiasis.**]—*Bull. Méd. du Katanga.* 1935. Vol. 12. No. 3. pp. 109, 111–123, 125–132.

A general article dealing with the trypanosomes which infect the domesticated animals. It contains nothing new and requires no special notice here. *W. Y.*

LAUNOY (L.). Suite à l'étude clinique et à celle du traitement de l'infection expérimentale du chat, du lapin et du cobaye, par *Tr. Annamense.* [**Clinical and Therapeutic Studies on Experimental Infections of the Cat, Rabbit and Guineapig with** *T. annamense.*]—*Bull. Soc. Path. Exot.* 1935. Nov. 13. Vol. 28. No. 9. pp, 817–823.

From the work described in the present and a previous paper (1934), it appears that occasionally *T. annamense* infections of the cat can be cured with a single dose of 2 cgm. per kilo. of moranyl. Cure can usually be obtained with two injections of 3 cgm., but even 3 injections (3 cgm.+3 cgm.+5 cgm.) sometimes fail. Attempts to cure infected rabbits with tryparsamide (0·15 gm. to 0·5 gm. per kilo.) were not successful. In guineapigs cure was regularly obtained with doses of 40 cgm. per kilo. of tryparsamide.

A number of therapeutic experiments were carried out on infected guineapigs with the substance, m.amino-p.oxyphenyl-arsino-di-thiomalate of sodium. This trivalent arsenical compound is prepared by Gailliot and contains 11·64 per cent. of arsenic. The toxic dose for guineapigs is between 8 and 10 mgm. per 100 gm. of body weight. It was found that a dose of 5 mgm. per 100 gm. sufficed to cure guineapigs infected with *T. annamense.* *W. Y.*

LAUNOY (L.), PRIEUR (M.) & ANCELOT (A.). Préparation et étude d'une souche de *Trypanosoma Annamense* rendue arséno-résistante. [**Preparation and Study of an Arsenic-resistant Strain of** *T. annamense.*]—*Bull. Soc. Path. Exot.* 1935. Nov. 13. Vol. 28. No. 9. pp. 857–866.

Details are given of the production of an arsenic-resistant strain of *T. annamense* by the usual method of giving repeated sub-curative doses of tryparsamide to an infected guineapig. In this manner a strain was easily produced which resisted the maximum dose of 15 cgm. of tryparsamide per 100 gm. ; the curative dose for the normal strain is 4 cgm. per kilo. Experiments showed that this strain, which had

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been made resistant to tryparsamide in the guineapig, was resistant to a trivalent arsenical, and that the resistance was maintained when the strain was passed into mice. [As the authors remark in their general conclusions, this work confirms for *T. annamense* some of the observations made by the reviewer and his colleagues with *T. rhodesiense*.]

W. Y.

v. JANCSÓ (N.) & v. JANCSÓ (H.). Chemotherapeutische Wirkung und Kohlehydratstoffwechsel. Die Heilwirkung von Guanidinderivaten auf die Trypanosomeninfektion. [**Chemotherapeutic Action and Carbohydrate Metabolism. The Curative Action of Guanidin Derivatives on Trypanosome Infections.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Oct. 3. Vol. 86. No. 1/2. pp. 1–30. With 5 figs. [41 refs.]

Previous work having suggested that there was a relationship between the carbohydrate metabolism of trypanosomes and their susceptibility to chemotherapeutic substances [this *Bulletin*, 1935, Vol. 32, p. 702], the authors decided to follow up this idea by examining the influence on experimental trypanosomiasis in the mouse of the guanidin derivatives which give rise to hypoglycaemia. It was thought that if the curative action of germanin really depended upon an interference with the carbohydrate metabolism of the trypanosomes, then it was possible that substances which were well known to affect sugar metabolism might prove to exercise a definite chemotherapeutic action.

The guanidin derivatives used were synthalin, synthalin B, monoguanid and thioguanid. The experiments were performed on white mice infected with various strains of *T. brucei*, *viz.*, (1) An arsenic-fast variety of nagana " ferox," (2) a normal strain of nagana " Prowazek," and (3) a germanin-fast strain prepared from Strain I.

It was found that synthalin acted most powerfully on Strains 1 and 3; in these cases cures could be obtained, whereas with the normal " Prowazek " Strain 2, as a rule, only a prolongation of the infection was obtained. This is very interesting because Strain 2 infections are readily curable by many chemotherapeutic substances, whereas Strain 1 is not only resistant to all arsenicals, but also to acridin and styrylquinolin-derivatives, and Strain 3 is in addition also resistant to germanin. The results of a number of experiments, which are summarized in tables, show that whilst the derivative synthalin exercises a curative action, the other derivatives have a comparatively feeble action.

Experiments were next undertaken to determine whether blocking of the reticulo-endothelial system (splenectomy+electro-colloidal copper) influences the action of synthalin. The results, which are given in a table, show that, whereas the normal mice infected with the arsenic-fast strain were all cured, the infections in the " blocked "animals were as a rule uninfluenced. The explanation given for this phenomenon is that the parasites are opsonized by the synthalin, and in the normal animals the opsonized parasites are removed from the circulation in masses by the phagocytes of the reticulo-endothelial system. This active removal of the weakened parasites from the circulation is one of the most powerful factors in the curative action of germanin and synthalin. Elimination of the phagocytes prevents the drugs from exercising their curative action.

Morphological studies in "blocked" animals showed that synthalin produces the same changes in the trypanosomes as germanin does; these are:—

(*a*) A slow cyclical degeneration of the flagellates.

(*b*) Fundamental morphological changes similar to those produced by germanin: firstly, an unusually large number of two nuclear division forms; then the characteristic micro- and macro-trypanosomes, and multinucleate giant forms, and finally bizarre degeneration and disintegrating forms.

The authors believe that synthalin acts directly, and that the continuous hypoglycaemia which it produces causes a sugar blockade of the parasites' metabolism. *W. Y.*

KLIGLER (I. J.) & COMAROFF (R.). **The Course of a Trypanosome Infection in Irradiated Rats.**—*Amer. Jl. Hyg.* 1935. July. Vol. 22. No. 1. pp. 11–17.

Experiments are described which suggest that daily exposure of rats for short intervals to direct solar irradiation fails to influence their resistance to trypanosome infection.

One group of rats was kept in an ordinary room in the animal house, another group in a dark room at the same temperature, and a third group in a dark incubator maintained at 29°–30°C. After acclimatization for 7 to 10 days the animals were exposed to direct solar irradiation. The exposure was made daily for 10 to 15 minutes between 11 a.m. and 1 p.m. over a period of 7 to 14 days. The rats were then infected and the daily exposure continued until death occurred. The effect of the irradiation was gauged by the duration of life after infection as compared with non-irradiated control groups kept under the same conditions.

The results of the experiments which continued over a period of two years and included 620 rats are given in tables. It appears that irradiation did not materially affect the resistance of the animals. *W. Y.*

RAFFEL (Sidney). **The Influence of Diphtheria Toxin on the Infection with *Trypanosoma equiperdum* in the Rat.**—*Amer. Jl. Hyg.* 1935. Sept. Vol. 22. No. 2. pp. 339–363. With 3 figs. & 1 graph. [45 refs.]

Consideration of the biological properties of the diphtheria toxin suggested that an investigation of the possible parasiticidal activity of this substance in a trypanosome infection of the rat might prove of interest. It was thought, for example, that there might be a direct activity of the toxin on the trypanosomes as animal cells, or alternatively that possibly the diphtheria toxin might exert some action on the protective elements of the host.

Albino rats were used in these experiments and were infected with a virulent strain of *T. equiperdum* by intraperitoneal injection of blood of passage mice. The diphtheria toxin employed was unusually potent containing 1,200 guineapig M.L.D. per cc. A second toxin, of which the L+dose was 0·2 cc., was used for purposes of confirmation. As a control for the activity of the toxin, this substance was heated to 70°C. for 45 minutes: according to RAMON (1923) such treatment destroys all toxic as well as anatoxic properties of diphtheria toxin. The elimination of toxicity by this method was confirmed by injection of large amounts into guineapigs.

The experiments are divided into two groups, the first dealing with the effect of the toxin *in vivo* and the second with its action *in vitro*. The technique used in the latter class of experiments was that devised by the reviewer and his colleagues (1929).

The following are the conclusions :—

"1. The injection of diphtheria toxin into rats infected with *Trypanosoma equiperdum* modifies the course of the infection. When it is injected intraperitoneally at about the time of infection, its influence is manifested as a prolongation of the incubation period, and in two instances, animals treated in this manner were freed of the infection. When injected intravascularly during the period of blood invasion, there is a marked decrease in the numbers of parasites in the blood and a subsequent "pseudo-relapse" in which the increasing trypanosomes are of a serologically unaltered character.

"2. The parasiticidal activity of the toxin *in vitro* is, so far as can be judged, much less marked than that of the pentavalent arsenicals or the *B. subtilis* "trypanotoxin" described by Levaditi and Twort, and is very far below that of the trivalent and arsenobenzol types of arsenic compounds.

"3. The results obtained in the infected animals appear incompatible with those observed *in vitro*. However, the evidence does not warrant the conclusion that the activity *in vivo* is partially the result of an auxiliary process, the immunity mechanism of the host. The fact that the immune response does not regularly take part here as with the use of the chemotherapeutic substances may be explained on the basis of the general lowering of the condition of the host and the specific lesions in certain of the reticulo-endothelial tissues which large doses of toxin occasion in the rat.

"4. The toxin does not decrease the infectivity of trypanosomes exposed to it. Neither does prolonged contact with this substance induce a resistance of the parasites to it, nor a change in their serological character."

W. Y.

Ascione (Guglielmo) & di Bello (Giovanni). A proposito dell' antagonismo fra tubercolosi e tripanosomiasi. Ricerche eseguite col B.C.G. ed il *Trypanosoma brucei*. [**The Supposed Antagonism between Tuberculosis and Trypanosomiasis. A Study of BCG and Nagana.**]—*Giorn. di Batteriol. e Immunol.* 1935. May. Vol. 14. No. 5. pp. 1073–1078. English summary (4 lines).

In 1914 Orsi stated that an antagonism existed between the human type of *Mycobacterium tuberculosis* and Nagana. He recorded that guineapigs infected with the trypanosome lost the infection when inoculated with the tubercle bacillus, and *vice versa* that guineapigs infected with tuberculosis did not sicken with trypanosomiasis when inoculated with the blood of animals containing the trypanosome.

The authors made three series of experiments using Nagana trypanosome and BCG. The strain of trypanosome was virulent, killing in 7–15 days, average 11 days. In the first series 18 guineapigs were used, 6 being inoculated with trypanosomes (one drop of blood from the ear of an infected guineapig was diluted to 1 cc. with physiological saline) intraperitoneally on the 10th, 12th and 14th August 1934. On the 16th two of each group were injected with 0·5 cgm. BCG subcutaneously another two intraperitoneally and six were kept as controls. They all died in 7–14 days, showing that here at least there was no antagonism.

In the second investigation 3 guineapigs were inoculated simultaneously with trypanosomes and 0·5 cgm. BCG subcutaneously, 3

intraperitoneally and 3 with trypanosomes only as controls. All died in 7–15 days. The simultaneous infection with both does not, therefore, give any signs of antagonism.

In the third series 5 guineapigs were given 1 cgm. of BCG subcutaneously and 5 had 0·5 cgm. intraperitoneally. A month later these 10 and three others for control were inoculated with the trypanosomes. All died between 7 and 13 days after the trypanosome injection. In other words, no indications could be observed of any protection afforded by BCG against infection by Nagana, contrary to what ORSI had found as regards the virulent human type of *Myco. tuberculosis* [see *Bulletin of Sleeping Sickness Bureau*, 1910, Vol. 2, p. 205]. *H. H. S.*

DUKE (H. Lyndhurst). **A Note on the Behaviour of Baboon and Monitor Blood in Tsetse Flies.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. July 31. Vol. 29. No. 2. pp. 207–209.

In the intestinal contents of *G. palpalis* which has fed on the baboon, *Papio tessellatus*, large masses of light green coloured crystals are found. The crystals persist for some days after the meal on the baboon. Two main types are found: long cylindrical crystals shaped like a whetstone or a needle, and a shorter form resembling Charcot-Leyden crystals, but round or oval in cross section. In flies fed on the monitor lizard (*Varanus ocellatus*) similar crystals are seen. No attempt has been made to study the crystals beyond the observation that they are soluble in ether. Duke concludes "It is remarkable that the two animals whose blood is richest in the substance responsible for these curious deposits are to all intents and purposes completely resistant to infection with the polymorphic trypanosomes by any normal route."

W. Y.

ROUBAUD (Émile) & TREILLARD (Marc). Un coccobacille pathogène pour les mouches tsétsés. [**A Cocco-bacillus Pathogenic to Tsetse.**]—*C. R. Acad. Sci.* 1935. July 22. Vol. 201. No. 4. pp. 304–306.

Pupae of *Glossina morsitans* were received in France by air mail, and though the adults emerged they died very quickly. Two were examined, and from one of them the authors isolated a cocco-bacillus, of which they here describe the principal cultural characteristics. They have difficulty in thinking how the organism could have gained entrance to the body of the fly, for which they feel sure it is pathogenic, but they do not discuss the possibility that the fly died of some quite different cause and that their organism is a post-mortem contamination.

P. A. Buxton.

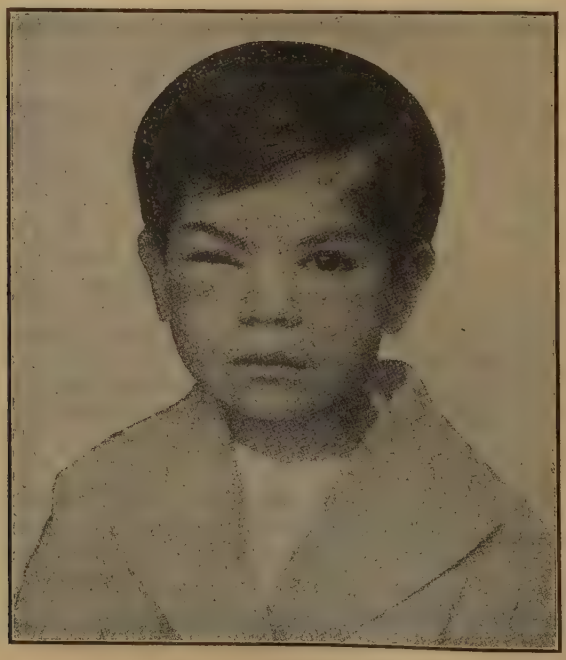
MAZZA (Salvador), GERMINAL & BASSO (Redento). Primer caso agudo de enfermedad de Chagas y primeros animales domésticos (perro, gato), portadores de *Schizotrypanum cruzi* comprobados en la provincia de Mendoza. [**First Case of Chagas's Disease reported in the Province of Mendoza.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy.* 1935. Publicación No. 24. pp. 3–16. With 6 figs. (3 maps).

The patient was a girl, 9 months of age, who two months previously had suffered from fever to 38–39°C., diarrhoea and vomiting, continuous sideways movement of the head and clonic contractions of the

right leg. The convulsive movements cleared up in a few days, but fever, diarrhoea and " meningeal irritation " continued. The face was noticed to be asymmetrical due to oedema of the left temporo-malar region and eyelids, with congestion and oedema of the palpebral conjunctiva. There was no thyroid enlargement. *Trypanosoma cruzi*, in small numbers, was seen on examination of blood. *Triatoma infestans* in the nymph stage were found infested in the dwelling, and dogs and cats in the houses of the district were found also to be infested. The presence of the parasite in the armadillo *Zaedyus pichy caurinus* had already been demonstrated by Dr. Mazza. *H. H. S.*

MAZZA (Salvador) & GOVI (Luis). Caso agudo de enfermedad de Chagas clínicamente denunciado en el Chaco por conjuntivitis esquizotripanósica unilateral. [**Chagas's Disease. An Acute Case in el Chaco.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy.* 1935. Publicación No. 24. pp. 19–27. With 8 figs. (1 map).

ROMAÑA has recorded unilateral conjunctivitis with oedema as an early sign of infection by *T. cruzi* and had, in fact, based on this the hypothesis that the conjunctiva may be a portal of entry. In the case recorded here the unilateral ocular condition directed attention to the possible trypanosomal nature of the disease. When examined, the patient, a child of 4 years, presented the appearance shown in the accompanying illustration. His temperature ranged to 40°C. with



Unilateral conjunctivitis with oedema as an early sign of infection by *Trypanosoma cruzi*.

[Reproduced from Publicación No. 24, *Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy.*]

morning remissions. Blood in smear revealed no trypanosomes, but they were seen in a thick drop preparation and the differential leucocyte count gave neutrophiles 38·6, lymphocytes 45·0, monocytes 15, eosinophiles 1·3. The liver extended 2 fingers'-breadths below the costal border, the spleen was just palpable. During the next week the oedema of the eyelids increased till the palpebral fissure was obliterated and the preauricular gland was enlarged. The log-hut in which the family dwelt was very heavily infested with *Triatoma infestans*. In one day's capture two nymphs and two adults were found with many metacyclic trypanosomes.

The patient was given sulpharsenol, starting with 0·06 gm., then at 4-day intervals 0·06, 0·12, 0·12, 0·12, 0·18, 0·18 gm., by which time the fever and oedema had disappeared. Trypanosomes could no longer be seen, but the liver remained enlarged, now 3 fingers'-breadths below the rib border. The differential leucocyte count was: neutrophiles 19·9, eosinophiles 4, basophiles 0·3, lymphocytes 61·3, large monoculears 14·3 per cent. *H. H. S.*

MAZZA (Salvador) & NASTRI DE FISCHER (Carolina). Investigaciones sobre la enfermedad de Chagas. II. Primeras comprobaciones de casos de enfermedad de Chagas en San Juan. [**First Proved Human Cases of Infection with** *T. cruzi* **in San Juan.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy.* 1935. Publicación No. 25. pp. 12–18. With 3 figs.

Two cases are detailed, both showing acute symptoms; one was a girl of 6 years and the other of 11 months of age. In the first the course of the disease was mild; the second died, "cause unknown," 6–7 weeks after the trypanosome infection had been discovered. One lived in San Juan itself, the other just outside. These are said to be the first human cases to be seen or recorded in the Province. *H. H. S.*

CÁCERES (Romeo) & IZAGUIRRE (Abelardo). Investigaciones sobre la enfermedad de Chagas. III. Primer caso de forma aguda de enfermedad de Chagas, determinado en la provincia de Entre Ríos y Litoral argentino. [**A Case of Acute Chagas's Disease in the Province of Entre Rios.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy.* 1935. Publicación No. 25. pp. 18–25. With 3 figs.

The patient was a boy, 5 years old. He presented the symptom which has been referred to before [see this *Bulletin*, 1935, Vol. 32, p. 717], as an early sign, *viz.*, localized oedema of the eyelids, malar and temporal regions, in this case the right side. Examination of blood smears revealed the trypanosome and animal inoculation gave positive results. Carotid and supraclavicular glands were enlarged, but not the thyroid. He was given "Paroxyl," a quarter of a tablet twice daily.

This is claimed to be the first case found in the Province of Entre Rios. [Existence of these cases is gradually being determined in one Province after another; it is possible that it is present more or less all over the Argentine.] *H. H. S.*

MINNING (Waldemar). Zur Spezifität der Komplement-Bindungs-Reaktion bei der amerikanischen Trypanosomiasis (Chagas-Krankheit). [**The Specificity of the Complement-binding Reaction in Chagas's Disease.**]—*Arch. f. Schiffs- u. Trop. Hyg.* 1935. Aug. Vol. 39. No. 8. pp. 315–328.

With the object of ascertaining the significance of the Machado reaction for the diagnosis of Chagas's disease, the author has employed the test with the sera from about 200 patients suffering from other diseases; he has also followed the reaction throughout the course of *T. cruzi* infections in dogs.

A detailed account is given of the technique used in preparing the antigen; this was made from the organs of young dogs which were infected when they were about 12 days old. The dogs, which were severely affected, were killed from 4 to 8 weeks after infection; the organ selected was ground up with sand, and to one part by weight were added 1 part of glycerine and 2 of water, and carbolic acid to the extent of 0·5 per cent. The extract was frequently shaken and kept at laboratory temperature for 5 days and was then filtered through gauze to remove the larger particles. The material was stored in the ice-chest. Guineapig serum, titrated in the usual manner, served as complement. The haemolytic system consisted of 1 cc. of 5 per cent. sheeps' corpuscles in 0·9 per cent. saline in combination with titrated amboceptor (1 : 1,000–1 : 1,500).

It was found that in man the reaction was not specific, as the sera of syphilitics, pregnant women, of women just after child-birth, of cases of pernicious anaemia, of hyperthyroidism and of worm infections gave a positive reaction in a high percentage of instances.

In a splenectomized dog the reaction was positive when parasites first appeared in the blood on the 9th day after infection, whilst in another non-splenectomized dog the reaction was not positive until later in the infection. It appears that during the course of the disease in dogs the reaction varies in a rhythmical manner, waxing and waning from time to time; a positive reaction was observed as late as the 349th day of the disease in one animal. It is noted that the Wassermann reaction was always positive when the Machado-reaction was positive.

W. Y.

NIIMI (S.). **Studies on Experimental** *Chagas* **Disease.**—*Japanese Jl. Experim. Med.* 1935. Aug. 10. Vol. 13. No. 4. pp. 543–564. With 6 coloured figs. on 1 plate. [21 refs.]

This paper describes researches undertaken with the object of investigating the cause of anaemia in Chagas's disease.

The strain of trypanosomes used in this work was brought from Brazil in 1932, and has been maintained by passage through mice. In the later passages it was found that the incubation period was shortened. The younger the animals the more serious was the disease. The infection in splenectomized rats did not differ from that in normal animals.

The blood changes were studied in infected young rabbits fed on a standard diet. The red cell count gradually fell; in 1 to 2 weeks it had decreased by about a million, and by the 7th week it had fallen by three millions by which time the animals were moribund. The haemoglobin value fell *pari passu* with the red cell count. The reticulocytes

increased at first, but decreased in number in the final stages of the disease. Polychromatophilic erythrocytes increase during the anaemia, but decrease remarkably at the end of the disease. Nucleated red cells, Howell-Jolly's corpuscles and poikilocytes are not very numerous, and thrombocytes decrease to a marked extent. Leucocytes at first increase and then gradually decrease in number; in the final stages there is a definite leucopenia. The haematopoietic organs were examined and showed histological changes quite in accord with these changes in the blood.

In the second portion of his paper the author considers the cause of these blood changes seen in *T. cruzi* infections. He cultivated the parasite on a medium consisting of equal parts of 2 per cent. broth-agar and of defibrinated horse blood. After allowing the parasites to grow for 20 days at 23–25°C., the condensation fluid was removed, centrifuged, and then filtered through a Chamberland L_5 filter in order to free it completely of trypanosomes. If this fluid is inoculated intravenously in a dose of about 2·0 cc. daily, all the blood changes noted above are produced. Inoculation of the trypanosomes themselves, freed from medium by washing in saline and killed by heating to 56°C. for 30 mins., failed to produce any anaemia.

In order to ascertain whether the culture fluid in the trypanosome bodies was possessed of antigenic properties, rabbits were immunized with repeated injections of each of these substances. They were then tested by intravenous injection of large doses of culture fluid. It was found that the animals which had previously received the small doses of culture fluid were protected against the harmful effect of the large doses, whereas those which had had the trypanosomes were rendered anaemic by the subsequent injection of culture fluid in just the same way as normal animals. Apparently, therefore, filtered culture fluid is possessed of antigenic properties, whilst the trypanosome bodies do not contain these substances. *W. Y.*

MAZZA (Salvador) & DRIOLLET (E.). Investigaciones sobre la enfermedad de Chagas. I. Comprobación de otra especie de armadillo en San Juan con infección natural por *Schizotrypanum cruzi*. [**Another Species of Armadillo found Naturally Infected by** *T. cruzi*.] —*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy*. 1935. Publicación No. 25. pp. 3–11. With 11 figs.

The authors examined six specimens of *Chaetophractus vellerosus pannosus* Thos. in Cochagual, which is 60 kilometres south of San Juan, Sarmiento Province, and found them heavily infected with *T. cruzi*, the leishmanial forms being abundant in the heart and the striped muscles. This makes four species found naturally infected in the Argentine, the others being *C. vellerosus vellerosus*, *Dasypus novemcinctus* and *Zaedyus pichy caurinus* [see this *Bulletin*, 1935, Vol. 32, p. 717]. *H. H. S.*

BONNE (C.). Over de Crithidiën van *Triatoma rubrofasciatus* de Geer. Eerste mededeeling. [**On the Crithidia in** *Triatoma rubrofasciatus*.] —*Geneesk. Tijdschr. v. Nederl.-Indië*. 1935. Aug. 20. Vol. 75. No. 17. p. 1490. With 1 plate.

Referring to the paper by MALAMOS [this *Bulletin*, Vol. 32, p. 718] recording the presence of *Trypanosoma cruzi* in monkeys from the

Dutch East Indies the author states that he has examined monkeys with negative result but has produced a trypanosome infection in mice by the inoculation of the crithidia which occur in the hind gut of *Triatoma rubrofasciatus* in Batavia. A similar observation was made long ago by LAFONT (1912) with the flagellates from this bug in Mauritius.

C. M. Wenyon.

MALARIA.

CHRISTOPHERS (S. R.). **Malaria Survey.**—*Riv. di Malariologia.* Sez. II. 1935. Vol. 14. Supp. to No. 3. pp. 87–95.

Malaria survey is of the highest importance because it is impossible to determine until the actual facts are known which measures of prevention should be adopted, or indeed if any preventive measures should be taken. The truth of this is demonstrated by several examples: the commonest anopheline in Bombay is *A. superpictus*, and this would certainly have engaged the attention of the health authorities had it not been for a malaria survey which showed that *superpictus* was harmless and that *A. stephensi*, which breeds in wells and cisterns, was the carrier. Owing to a religious tenet of the Parsees, wells must be so situated that light from the sky can reach the water. Owing to the density of population, communal houses several stories high are usual, and a type of dwelling has resulted in which the tiers of living rooms opening inwards are arranged around a central, narrow space, at the bottom of which is the open well. In other parts of the city, *A. stephensi* bred in household tanks and cisterns. In the course of years, almost all the wells in Bombay have been abolished or rendered mosquito-proof, and stringent regulations are enforced regarding the protection of cisterns. Other instances of the value of preliminary malaria survey, for example in the Punjab and the Andamans are given, and also an outline of the technique of survey work. *W. Fletcher.*

JAMES (S. P.). L'épidémie de paludisme à Ceylan en 1934–1935. [**The Ceylon Epidemic of Malaria, 1934–35.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. June. Vol. 27. No. 6. pp. 1135–1140. With 1 map & 1 diagram.

The island of Ceylon lies in the Indian Ocean between 5° and 10° North of the Equator. It is about half the size of England and has a population of 5½ million. About 60 per cent. of the population inhabit the humid, fertile south-west region which is traversed by the main rivers coming down from the central hills. It is in this region that the terrible epidemic has occurred. Malaria is always prevalent in Ceylon; even in normal years, about 1½ million malaria patients are treated at the hospitals and dispensaries, and the Government spends £23,000 a year on free quinine. Though there are many species of anopheles, *A. culicifacies* is the only active carrier. Benign tertian is the commonest type of malaria and quartan comes next, malignant tertian is comparatively rare. The dry, north-eastern zone of the island is normally the most malarious; the humid, south-western province is almost free from it, and in its plains the splenic index is usually about 5 per cent. as compared with 70 per cent. in the dry zone. It had been noticed, in the past, that in dry years when the monsoon failed there was more malaria in the healthy humid zone, and, in 1934, when the south-west monsoon not only failed but was entirely absent, the authorities became alarmed and sent out warnings to the sanitary inspectors. A fortnight later, in the beginning of October, the epidemic began, and in November many of the dispensaries were treating ten times the usual number of malaria cases. By the middle of December, the epidemic reached its height; whole villages were struck down at once, roads were blocked by victims painfully making

their way to the hospitals and dispensaries and the medical department was treating 60,000 cases a day. The first wave of the epidemic declined with the new year and came to an end in March, but it was quickly followed by a second. This second wave was apparently due to recurrences, and not to fresh infections [but see GILL, below]. The vast majority of the infections were of the benign tertian type, and the production of late recurrences is characteristic of the benign tertian parasite. The case mortality, thanks to the comparative rarity of malignant tertian infections, was comparatively low ; for the whole of the affected zone it was some 1·5 per cent., while it was about twice this figure at Kegalle which was the centre of the epidemic.

The primary cause of the epidemic was the complete failure of the south-west monsoon. Instead of the summer rains, there was drought from May to October. This had no effect upon the dry, north-eastern zone, which even in normal years is not reached by this monsoon, and the malaria there during 1934–5 was no worse than usual ; but the effect upon the humid south-western zone was disastrous. There, the large lakes dwindled until each one became a collection of small shallow ponds, and the big rivers sank until nothing remained but a series of clear pools. The result was a veritable plague of mosquitoes ; *A. culicifacies* swarmed into the houses, and spread malaria. The infection rate of mosquitoes caught in houses over the whole region was 14 per cent. The drought was not only responsible for the plague of mosquitoes, but also for a failure of the crops which brought the population to a state of poverty and malnutrition and made them readier victims. Another factor which favoured the epidemic was the absence of immunity in the south-western zone where malaria is uncommon and the people are not used to dealing with it. The author pays tribute to the central, municipal and charitable organizations for the energetic steps which they took to limit the effects of the epidemic. To have prevented it, even with unlimited funds and a very large staff, would have been an impossible task. It is one thing to control malaria in a small town or plantation, but quite a different matter to suppress mosquito breeding in thousands of pools in the beds of large rivers and their affluents, let alone those in the lakes and marshes. (See also WIGGLESWORTH, this *Bulletin*, 1935, Vol. 32, p. 732.)

W. F.

CEYLON. Sessional Paper XXIII.—1935. **Report on the Malaria Epidemic in Ceylon in 1934–35. Together with a Scheme for the Control of Malaria in the Island** [GILL (C. A.), Expert Adviser on Malaria to the Ceylon Government].—44 pp. With 7 charts, 9 maps & 11 photographs. 1935. Sept. Colombo : Govt. Record Office. [Rs.3.]

The epidemic was not due simply to excessive mosquito breeding and to poverty resulting from the drought, but to the presence of these conditions simultaneously with the presence of an X factor which occurs periodically every 5 years and is associated with the malaria parasite. [Apparently a recurring high virulence or swarming of the malaria parasite.]

Colonel C. A. Gill, I.M.S., formerly Chief Malaria Officer, Punjab, was commissioned by the Government : (1) To review the recent epidemic and to consider its probable consequences. (2) To review the anti-malaria work carried out in Ceylon during the last 12 years.

(3) To define the future policy in regard to malaria in Ceylon. (4) To formulate the scope and powers of an Anti-Mosquito Ordinance.

He arrived in Ceylon at the beginning of April, 1935, and remained for about 5 months. He has drawn up his report in two parts: the first is a general review of the epidemic, the second embodies a scheme for preventing the occurrence of epidemics in the future.

Epidemics of malaria occur in Ceylon at intervals of about 5 years, but that of 1934–5 was the greatest pestilence in the recorded history of the island and destroyed 80,000 lives in the space of 7 months. The great epidemic of 1867 in Mauritius is the only instance of an epidemic in the tropics which can compare with it. The Ceylon epidemic, so far as mortality is concerned, comprised a great primary wave which started in November 1934 and reached its height in the middle of January. It was followed by a smaller wave in May 1935 which was still declining in July. This second wave was associated with a rise in the infection rate of anopheles, and "it was therefore a true epidemic wave being due, in part, to new infections as opposed to relapses." Ceylon had been particularly healthy for some years before the epidemic; there had been a conspicuous downward trend of the death rate for 10 years and more especially for the last 5. The death rate for 1932 (20·5) was the lowest on record. The actual onset of the epidemic was preceded by an increase of out-patients at some of the dispensaries during the latter half of September; a fortnight later the same thing occurred over a wider area and, at the end of October, the epidemic began with an explosive outbreak which occurred, almost simultaneously, over an area of about 5,800 square miles. This area comprises the healthy, populous western quadrant of the island known as the "wet zone" in contradistinction to the dry zone in the north where malaria is hyperendemic (see JAMES above). Throughout this area, almost the whole of the 3 million inhabitants, already enfeebled by famine, the result of a drought caused by failure of the south-west monsoon, were suddenly overwhelmed with sickness. The epidemics of the past have occurred in the same area, and have also been associated with drought. Malaria in the dry, northern zone is, on the contrary, associated with excessive rainfall.

Colonel Gill is full of admiration for the way in which the epidemic was dealt with by the Medical Department; he writes of "the prompt and thorough manner in which it was tackled . . . the able manner in which the scheme was organized and administered by the Head of the Medical Department, and, it may be added, the splendid response made by all members of the Medical and Sanitary Departments to the heavy demands made upon them." There was never any shortage of quinine.

A. culicifacies, the anopheline carrier of Ceylon, is essentially a dry zone species, widely prevalent in the north and east of the island where malaria is hyperendemic. It is much less prevalent in the comparatively healthy wet zone. In former epidemic years it has been found spreading southwards into the wet zone and during the recent epidemic it was found in vast numbers much to the south of its normal habitat, more particularly in the neighbourhood of the rivers. Mr. H. F. CARTER, the Entomologist, has found that, in years when the monsoon is normal, these rivers do not act as breeding grounds for *A. culicifacies* because they are subject to repeated flushing, but in years of deficient monsoon rainfall, such as 1934, the

full-flowing river is replaced by a series of rocky pools which constitute a favourite breeding place of this mosquito. Observations made before and during the epidemic showed that the pools and sheets of water in the river beds contained *A. culicifacies* in prodigious numbers, and it was in their vicinity that the epidemic first appeared and subsequently attained its maximum intensity. Colonel Gill does not think that the phenomenal breeding of anopheles in the river beds was the sole factor concerned. He points out that epidemics in Ceylon and many other countries tend to recur at intervals of 5 years or multiples thereof, and he considers that periodicity plays an important part. This periodicity is presumably an attribute of the malaria parasite, the quality known as the "X factor" of Pettenkofer or the "epidemic potential."

In 1934 a periodical epidemic was due and, at the same time, several other things happened to occur simultaneously which were favourable to the spread of malaria: (*a*) a population which was non-immune after a series of exceptionally healthy years; (*b*) a drought which caused poverty among the population and brought about an abnormal proliferation of mosquitoes. The drought alone would not have caused the epidemic; droughts occur at irregular intervals in Ceylon and they are not always associated with epidemic malaria, but, in 1934, the drought and the X factor and the non-immune population happened to be present at the same time. The X factor did not cause an epidemic in the dry hyperendemic zone of the north because the population of that part of the island is relatively immune. Again, the X factor was unable to cause an epidemic in the southern zone, although there were many non-immune children there and although the drought had the same effect upon the rice crops and the rivers as it had in the epidemic area. This freedom of the southern zone, Colonel Gill ascribes to the absence of endemic malaria—the spleen rate is only 0·5 per cent.—and to the scarcity of *culicifacies*. He concludes that "by broadening the basis of the existing hypothesis in regard to the mechanism of malaria epidemics so as to ascribe a larger part in their causation to a periodicity pertaining to the malaria parasite, it is possible to provide a satisfying explanation of the remarkable characteristics of the Ceylon epidemic."

Colonel Gill studied and reported on the antimalaria work which has been carried out in Ceylon during the last 10 years or so. The measures included levelling, the stocking of ponds and wells with "millions," the treatment of water collections in the protected and controlled areas with oil or Paris green, and the provision of drains (mostly earth drains) for the removal of storm water. He found it most difficult to judge the amount of success achieved. The 5 years preceding the epidemic were exceptionally healthy, and it was therefore hard to say how much improvement was due to antimalaria measures. Another point is that in a place where the spleen rate has been reduced by antimalaria measures from, say, 60 per cent. to 30 per cent. the communal immunity has also been reduced and the proportion of children increased, and on this account an epidemic is likely to be more severe than if the spleen rate had remained at 60. "The organization of the Malaria Department, as well as the technique of anti-malaria operations, is in all respects admirable, and, if it cannot command success, it certainly has deserved it. . . . Taking all things into consideration it seems justifiable to infer that the control schemes have achieved a certain measure of success at Chilaw,

Puttalam, and Trincomalee, but it is doubtful whether they have had much effect elsewhere. The restricted measure of success does not however reflect upon the measures and methods employed or upon the manner in which they were executed; the main reason is undoubtedly the slow progress made with the drainage schemes on account of lack of funds."

The second part of the Report deals with recommendations for the control of malaria in Ceylon. Colonel Gill expects that the effects of the epidemic will gradually disappear and that there will be no serious outbreak until that due in about 1940. Epidemics once started are uncontrollable, but he believes that it will be possible to prevent their occurrence by the steady prosecution of antimalaria measures *during interepidemic periods*—" epidemic malaria is epiphenomenon of endemic malaria, from which it follows that measures that will reduce the incidence of endemic malaria will also prevent the outbreak of epidemics." [This is hard to reconcile with the statement in another part of the report that the reduction of the spleen rate from 60 to 30 per cent. would make an epidemic more dangerous by reducing the communal immunity.] The measures recommended are designed to eradicate the malaria-carrying mosquito, to reduce the number of human carriers, to alleviate economic stress and to improve hygienic conditions.

The main principle of Colonel Gill's scheme is that, where possible, malaria control should be entrusted to the local authorities, who would be given such financial and technical assistance as might be necessary. The scheme depends for success, he says, upon public opinion. He proposes the enactment of an Anti-Mosquito Ordinance which will make occupiers of property responsible for the execution of antimalarial measures, and empowers the Government, in default, to carry out the work at the cost of the occupier. He endorses the proposal to erect a Malaria Research Institute in commemoration of the Jubilee. Its function would be to carry out research and to give advice on all matters connected with malaria. Other important recommendations in his scheme are the creation of local public organizations under Medical Officers of Health, and the creation of a Sanitary Works Board to assist the local bodies, by grants in aid, to execute water supply and drainage schemes. The Director of Medical and Sanitary Services would exercise general supervision, and the staff of the Research Institute would give technical advice. It is strongly emphasized that malaria control should be part of the work of the public health branch of the Medical Department. In rural areas, " apart from simple measures that can be carried out by an intelligent sanitary inspector and the provision of ample facilities for the treatment of malaria . . . the only measures that can be suggested for controlling malaria . . . are general schemes for promoting rural betterment, more particularly land drainage schemes, irrigation schemes, and development schemes. . . . it is recommended that Government should assume responsibility for carrying out such measures as may be found, after investigation, to be practicable to control mosquito breeding in these rivers." As regards the control of malaria on estates, legislation is recommended making it obligatory upon the Superintendents to carry out all reasonable antimalaria measures. Colonel Gill draws attention to several matters of detail, some of which are of vital importance; it is necessary, for example, that the hospitals should be provided with microscopes and that the

medical officers should be instructed how to use them for the diagnosis of malaria. It is equally necessary that the stock mixtures of quinine should be standardized in order to ensure that proper treatment is given. *W. F.*

CEYLON. Sessional Paper XXII.—1935. **The Ceylon Malaria Epidemic, 1934–35. Report by the Director of Medical and Sanitary Services** [BRIERCLIFFE (R.)].—96 pp. With 15 photographs. Supplement to Sessional Paper XXII.—1935. **Maps and Charts.** 20 maps & 8 charts. 1935. Sept. Colombo: Govt. Record Office. [Rs.4.50.]

Details are given of several cases in which death followed the administration of atebrin musonate.

This classical account of the Ceylon epidemic written by Dr. R. Briercliffe, Director of Medical and Sanitary Services, was largely compiled from information supplied by different officers of his Department; it deals with events up to the end of April, 1935. During April and May, a secondary wave of malaria swept over the epidemic area which will be dealt with by him in a future paper. A compilation from the same sources by Col. S. P. JAMES has been summarized above, and consequently this summary of Dr. Briercliffe's report is limited to matters such as the results of treatment with atebrin musonate.

A comparative test of atebrin musonate and quinine was made in the hospitals during April 1935. A group of 681 patients was given two intramuscular injections of 0·375 gram of atebrin musonate, with an interval of 24 hours between them. A second group of 424 patients was treated with two intramuscular injections of 15 grains of quinine, followed by quinine given by the mouth. Nearly a quarter of the patients in the atebrin group, as compared with more than a third of those in the quinine group, complained of pain at the site of inoculation; there were two abscesses in the atebrin group, but none in the quinine group. There were more deaths in the atebrin group, and 4 of the 17 which occurred in this series were attributed directly to atebrin. One of the patients was a young adult who collapsed and died 4 hours after her first injection. The other three were children; the first, aged 8 months, collapsed immediately after the injection and died 16 hours later; the second, aged 4 years, collapsed and died 4 minutes after the first injection; the third, aged 2 years, died a few minutes after the second injection.

Between May 20 and May 31, 1935, 1,387 persons in malarious villages were treated with atebrin injections; 61 suffered from toxic symptoms such as vomiting, collapse and abdominal pains. Mental symptoms, which in most cases lasted for about a week, occurred in 8 patients and one of them died from exhaustion. Pain at the site of inoculation was complained of by most of the patients, and in 9 abscesses resulted. The data available did not allow definite conclusions to be drawn with respect to the relapse-rate, "but the impression exists that a full course of atebrin by mouth (1·5 grams) has a greater effect in preventing the return of fever than a week's careful treatment with quinine, and that either of these courses of treatment is superior in this respect to two injections of atebrin musonate."

The following conclusions were reached from a study of the reports from hospitals and dispensaries in the epidemic area: "Probably in rather more than a half per cent. of the hospital patients treated with atebrin musonate death has been attributed to the drug. The greatest

care is necessary in the selection of patients for treatment . . . Small children have been specially liable to develop sudden collapse or convulsions. . . . The majority of patients suffering from malaria do not require to be treated with injections, whether of quinine or atebrin. When, however, treatment by injection is indicated, quinine is to be preferred to atebrin on account of its greater safety." Among adults, pregnant women have been found particularly liable to collapse after the injections. Sometimes symptoms of chronic or delayed atebrin poisoning which were attributed to faulty excretion of the drug appeared towards the end of a course of treatment. The temporary mental derangement which may result from the administration of atebrin proved a serious objection to its use ; in one district, where several hundred people had been treated with oral atebrin, at least 15 cases occurred and the use of atebrin was abandoned.

Colonel C. A. GILL writes in his report, which is summarized above that

" It is possible that the relative frequency with which toxic (cerebral) symptoms and abscesses at the site of injection are reported to have followed the administration of atebrin musonate during the epidemic is attributable to the low state of vitality of many of the patients. In these circumstances it is doubtful whether any experiment with atebrin musonate carried out in Ceylon during the epidemic is calculated to throw light upon its value under normal conditions."

The course of the epidemic can be followed in the Press Communiqués which were issued by the Ministry of Health, and of which copies are printed as an appendix to the Report. The hospital deaths and admissions for malaria were : October, 1,584 cases, 32 deaths ; November, 4,178 cases, 65 deaths ; December, 14,480 cases, 381 deaths. The amount of malaria in the epidemic area began to decrease during the last week in December ; throughout January and February the decline continued, and in March it became even more rapid, but in April the situation became less favourable owing to localized outbreaks.

Extensive anti-larval measures were started in January. The oiling of breeding places in the beds of the main rivers and their larger tributaries was undertaken where *A. culicifacies* larvae were found to be prevalent, and 300 miles were brought under control. The Report contains some good photographs of the rock pools in the bed of the Maha-oya, Ceylon's largest river, which were breeding places of *A. culicifacies*. The following is taken from a communiqué issued by the Ministry of Health :—

" The Department wishes to make it clear that the mosquito which is carrying malaria in Ceylon, viz., *Anopheles culicifacies* is not breeding in roof gutters, coconut shells, cans, etc., but in open pools of clear water, in river beds and in rock quarries. It may also be found in shallow wells, brick pits, borrow pits, saw pits, etc., where the water is clear and exposed to sunlight. It does not breed to any great extent in paddy fields or swamps." *W. F.*

DICKSON (R. M.). **The Malaria Epidemic in Ceylon, 1934–35.**—*Jl. Roy. Army Med. Corps.* 1935. Aug. Vol. 65. No. 2. pp. 85–90.

The author directs attention to the poverty and distress caused by the drought and to the measures taken to alleviate these and combat the epidemic of malaria.

Col. JAMES's report of this epidemic has already been summarized. The present paper deals more fully with the measures taken. The medical authorities always keep a reserve supply of quinine equal to 10 months' normal requirements; more than 7,000 lb. were available at the beginning of the epidemic and additional supplies were quickly obtained. The State Council approved the formation of a Malaria Relief Fund. The Government contributed 300,000 rupees and the public about 45,000. Local Relief Committees were appointed and these were responsible for the distribution of rice and foodstuffs. At the dispensaries in the worst areas, Horlick's malted milk was distributed to the children, and food kitchens were established by voluntary agencies. "Distress and destitution are likely to increase for some time to come, but relief measures are now well organized and are sufficient to meet the situation." [See also S. P. JAMES, BRIERCLIFFE and GILL, above.] *W. F.*

FEDERATED MALAY STATES. **Annual Report of the Malaria Advisory Board for the Year 1934** [KINGSBURY (A. Neave), Chairman].—27 pp. 1935. Kuala Lumpur: F.M.S. Govt. Press.

This contains an important report on drain flushing as a method of larval control. It also contains a good summary of antimalarial work done in connexion with fish-ponds in Java, and notes on *A. umbrosus* and *A. barbirostris* as carriers in the Federated Malay States.

A committee appointed by the Board to inquire into the utility of sluicing as an antilarval method in Malaya reported that:—

"Sluicing has not so far been found dependable in preventing the breeding of larvae in those seepages and small water channels which form the principal breeding places of *A. maculatus*. In small streams running in firm soil, in those streams in flat land which require treatment, but pre-eminently in streams running over rock, sluicing is likely to prove of value in antimalarial work. Sluicing is unsuited to use in streams in the more friable soil characteristic of a great part of the country. In these streams the rapid erosion caused by sluicing results in undercutting of the banks, the formation of numerous side pools and silting up of the reservoirs. . . . It is considered that sluicing is unlikely to prove of sufficient general application to warrant further *expensive* experiments by this Board."

In the Cameron Highlands, where Professor Williamson first reported the successful employment of sluice-gates, further investigation showed that "the use of temporary gates here on a large scale has not been sufficiently successful, either economically or in preventing larval breeding, to justify the method replacing oiling control." Sluicing was tested over a period of 11 months in the town of Lipis, in Pahang, and the Health Officer reported: "Chinese squatters living in the ravine while sluicing was employed developed malaria for the first time; when oiling was resumed no more cases of malaria occurred." On the other hand, considerable success has been claimed for the method in Province Wellesley and in the Island of Penang. (See this *Bulletin*, 1934, Vol. 31, p. 153 and 1935, Vol. 32, p. 429).

Dr. B. BARROWMAN drew attention to an increase of malaria in the flat coastal districts of the west coast where *A. umbrosus* is the carrier. Clean drains and clean weeding had controlled the breeding of this mosquito, but owing to hard times weeding had been neglected and drains had become blocked. The shade necessary for the breeding of this mosquito could be provided by vegetation only a few inches

high. It was not enough merely to fell heavy jungle; the entire surface had to be clean weeded.

Dr. R. S. JOHNSTON reported on endemic malaria in the township of Batu Gajah, where it has been found that *A. barbirostris* is the vector.

Dr. J. C. P. GREY who had paid a visit to Java in order to study the methods of malaria control adopted there, gave an account of the different methods by which the fish-ponds are treated in order to prevent mosquito breeding. He stated that "It had been in many ways curious, after experience in Malaya, to see the light-hearted treatment accorded to *A. maculatus*. In no place was its control by anti-malarial oiling or by subsoiling observed." *W. F.*

SWELLENGREBEL (N. H.). **The Basis of Malaria Control by Antilarval Measures in the Netherlands.**—*Malayan Med. Jl.* 1935. Sept. Vol. 10. No. 3. pp. 61–66.

Professor Swellengrebel has the gift of lucid exposition. This is a delightfully clear account of the spring epidemic of malaria in northern Europe and of the different types of *maculipennis*. It should be invaluable to lecturers and students, and has been summarized rather fully for this reason though it covers ground which has been covered already by papers previously summarized in this *Bulletin*.

The only species of Anopheles in Holland is *A. maculipennis*. It is present throughout the whole country, but malaria is limited to the coastal provinces. It does not occur in all of them; the province of South Holland is just as watery and low-lying as the others, yet it is free from malaria while the adjoining province, North Holland, is the most malarious area in the country. The problem which faced the author on his return from the East in 1919 was to discover the reason for this, and here he tells how it was done.

Benign tertian malaria occurs every year in North Holland and, in epidemic years, as many as one-fifth of the total population may be attacked. The epidemics occur about every twenty years and they last for 3 or 4 years. The highest incidence of malaria is in May, June and July. During the period January to August of the epidemic year 1920, the author dissected a large number of mosquitoes caught in houses where malaria was rife, but he found hardly any infected specimens and would have given up the search in disgust had he not been dissuaded by his friend Dr. Korteweg. Korteweg had been practising for many years in a malarious village north of Amsterdam; every spring he had seen a number of primary cases of malaria at a time when there were no mosquitoes about, and he came to the conclusion that these spring cases were the result of infections which had been acquired in the previous autumn and had remained latent throughout the winter. The number of cases of malaria in Holland varies inversely with the number of mosquitoes present at the time; in the spring, when there are no mosquitoes, the greatest number of malaria cases occurs. During the period September to February, when there are no malaria cases, the greatest number of anopheles are found in houses. Swellengrebel was persuaded by Korteweg to continue his dissections in the autumn and winter, when the malaria season was over. He writes:—

"Although I had little faith in dissecting anopheles at the tail-end of the malaria season, I did as Korteweg told me. Well, it gave me the thrill

of my life. Here they actually were—the infected anopheles, which I had been vainly looking for in summer. Three per cent. of all the mosquitoes collected in September were infected ; 5–6 per cent. in the other months of the year 1920, and a lower percentage in January till March. Then the infection stopped. . . . Why did I not find infected anopheles in summer ? For two reasons : first, because these anopheles do not usually feed on man in summer, but they do in autumn. Catching anopheles in houses in summer and selecting the engorged females, yields one only with human blood out of every ten tested. But from September onwards eight or nine out of every ten tested have bitten man. That is one reason. The other is that infected anopheles in summer are creatures of a short life. There is a heavy mortality among them. But as soon as egg-laying stops, and that happens by the beginning of September, the mortality sinks from over 60 dying within 4 weeks out of a batch of a hundred, to no more than 20 dying within 4 weeks out of a batch of a hundred."

Though infected anopheles are most numerous in the autumn the malaria season does not occur until the following spring. Korteweg's hypothesis that the infections, transmitted to man in the autumn, remain latent until the spring, was confirmed by James in England and by the author and his colleagues in Holland, where 8 volunteers who were bitten experimentally by mosquitoes in the autumn first showed signs of malaria in the following spring and summer.

The author found that during the season of transmission, that is during the autumn and winter, the warm houses and stables contained many anopheles which were wintering there. These "winterers," as he calls them, continued to suck blood although they had ceased to lay eggs and therefore had no need to leave their shelters. In some districts, the anopheles sought cold lofts and sheds in which to pass the winter, rather than the warm houses and stables. These anopheles were in a state of hibernation ; unlike those in the warm shelters, they did not continue to feed after they had ceased to lay eggs. A map was prepared showing the distribution of the *winterers* and the *hibernators* throughout the Netherlands in autumn and winter. It then came out that the winterers preponderated in the malarious coastal districts and the hibernators in the healthy inland districts. As regards the one healthy coastal province, South Holland, there too the anopheles were hibernators, while in the malarious provinces of North Holland, to the north, and Zeeland to the south, they were winterers. In all these provinces the anopheles breed in the ditches, but South Holland is the delta of the Rhine and Meuse and its ditches contain fresh water. The malarious province of North Holland has the North Sea to the west, and the Zuyder Zee to the east ; no rivers carrying fresh water run through it and consequently the water in the ditches is brackish. The malarious provinces are characterized by the presence of winterers and of breeding places containing brackish water ; but in the healthy provinces, the anopheles are hibernators and the breeding places contain fresh water.

Is there a fundamental difference between the winterers and the hibernators ? The two types were collected separately in their winter quarters and kept in the laboratory until they laid their eggs and until these produced larvae. It was then found that there were morphological differences between the eggs and larvae of the winterers on the one hand and of the hibernators on the other. The winterers will breed in captivity, and it was soon established that the egg and larval characters remain constant from generation to generation.

The hibernators will not breed in captivity, but male hibernators will mate with female winterers, and male winterers with female hibernators; it has been found, however, that the eggs which result from these cross-matings rarely hatch, and, if they do, the larvae all die within 24 hours. The winterers and the hibernators are therefore *sexually isolated*; they are, indeed, constant species. More recently it has been found possible to distinguish the adult winterers from the hibernators, during the autumn and winter, by the shape of their salivary glands. Consequently they can now be separated in cases where they are both occupying the same winter quarters, as they do in attic bedrooms. Here they are not segregated as they are in warm rooms and stables on the one hand, and in cold lofts and sheds on the other; in the attics, both types find what they need; blood for the winterers and a low temperature for the hibernators. The hibernators never touch blood and are never infected, though they may be perched on the same wall as the winterers which, in some houses during the autumn of 1934, were found infected up to a maximum of 25 per cent. [see DE BUCK and SWELLENGREBEL, below.]

The author and his colleagues next discovered that the different types preferred different places for breeding purposes. They examined over 1,400 breeding-places and over 23,000 larvae, and they came to the conclusion that the hibernators preferred fresh water with less than 500 milligrams of chlorine per litre, while the winterers (*A. maculipennis atroparvus*) preferred brackish water with a salt content of more than 1,500 milligrams of chlorine per litre. The malarious province of North Holland has sea on both sides and brackish water in its ditches; but the sea on the east side has now been cut off from the open sea by a dam, and, as the river Yssel flows into it, it is gradually becoming less brackish. This is a part of the Zuyder Zee reclamation scheme now in progress. It is hoped that this fresh water lake can be used to reduce the salinity of the surface water in North Holland to a harmless level; when this has occurred it is expected that the hibernators will invade the province at the expense of the malaria-carrying winterers, and that malaria will gradually disappear.

W. F.

LUTRARIO (A.). La malaria en Italie. [**Malaria in Italy.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. June. Vol. 27. No. 6. pp. 1141–1160. With 2 charts.

Many papers have been written about malaria in Italy, and many of them have been summarized in this *Bulletin*. The present paper deals with the subject in an interesting and comprehensive manner, and the author demonstrates clearly the remarkable decline of malaria in Italy during the last 50 years, particularly since the application of the malaria laws and the systematic distribution of quinine.

He draws particular attention to the rhythmical rise and fall which occurs in malaria. Small cycles which coincide with the yearly seasons, larger ones with periods of 4 or 5 years, and others yet larger whose duration is to be measured in centuries. These large cycles are demonstrable in the history of Rome. In its early days it was free from malaria, but in the third century B.C. the disease appeared in epidemic form. At the beginning of the present era, Rome was once more healthy, but in the sixth and seventh centuries malaria was again severe. In the eighth century there was a remission, and

Mean annual death rates per million from malaria in Italy from 1887 to 1930. [Reproduced from the *Bulletin de l'Office International d'Hygiène Publique.*]

prosperity returned to the country; in the ninth, the country was once more devastated by malaria. The next period of relative freedom appears to have been at the time of the Renaissance, but from 1600 to 1750 malaria was again severe. Then once more there was an amelioration until the nineteenth century when malaria increased again. From the year 1879 onwards, there was a tendency to spontaneous regression which is apparent in the accompanying graph.

The graph also shows in its earlier part the cyclical exacerbations which occur every 4 or 5 years, and demonstrates how these have been suppressed since the quinine laws were instituted at the beginning of the present century. Subsequent to the manufacture and free distribution of quinine by the State, the death-rate per million from malaria sank from 417 in 1900 to 57 in 1914. *W. F.*

COLONIAL DEVELOPMENT FUND (MALARIA RESEARCH SCHEME). **Report on Work done at Dar es Salaam during the Period January 1932–January 1934** [MACKAY (Roderick), Malaria Research Officer].—79 pp. With 13 charts & 4 folding plans. [11 refs.] 1935. London: Crown Agents for the Colonies, 4 Millbank, S.W. 1. [10 Shs.]

Of special general interest are an outbreak of poisoning following the use of Paris green, a number of cases of congenital malaria, and the finding of *A. costalis* in brackish water.

Dr. Mackay's report on this very thorough survey of Dar-es-Salaam begins with a review of the investigations of KOCH and OLLWIG. In 1899 KOCH instituted an anti-malaria campaign by means of quinine. This work was continued for 12 years. Its effect was to reduce the total amount of malaria, but it was useless as a method of eradicating malaria. The town was only a fishing village in 1890, when the German administration was established. It lies in a valley half of which is below sea level; a tidal flap in an embankment constructed during the German administration prevents the ingress of the sea. The population totals 33,000 consisting of many different African tribes, two-thirds are Bantus. The examination of a random sample of 8,310 persons showed that 54·2 per cent. were infected. The parasitic index, in children, was 77·2 per cent. The commonest infection was subtertian; of 6,071 positive examinations, there were 4,069 or 66·9 per cent. subtertian, 969 or 15·9 benign tertian, 587 or 9·9 quartan, while 446 or 7·3 per cent. were not differentiated; these last included a small proportion of *P. ovale* and *P. tenue*. It seems likely that "the human host finds it easier to establish an equilibrium between himself and *P. vivax* or *P. malariae* species than is the case with *P. falciparum*, which alone persistently increases with advancing age . . . a considerable proportion of children are born with definite evidence of malarial infection contracted *in utero*; . . . 44 blood smears, taken from the peripheral blood of infants at birth, have yielded eight subtertian trophozites and one benign tertian gametocyte"; *Anopheles gambiae* (*costalis*) is by far the most important mosquito; *A. gambiae* and *A. funestus* were the only anopheles caught in houses. Out of 146 *A. gambiae* dissected, 6·8 per cent. were infected with sporozites; out of 179 *A. funestus*, 3·3 per cent. were infected. *A. gambiae* was found breeding not only in fresh water but also in water with a high saline content. It usually breeds in shadeless water while *A. funestus* prefers a degree of shade. An examination of anopheline stomach contents showed that 81 per cent. contained human blood. Other figures indicating the amount of malaria in the town are a spleen rate of 83·8 and an incidence of 5·9 cases of blackwater fever per 1,000 cases of malaria. The development of the parasite in the mosquito occupies 10 days in the wet season, but 21 in the dry season. A number of cases were given atebrin 0·2 gram and plasmoquine 0·02 gram daily for 8 days. Epigastric pain was

invariably complained of by adults towards the end of the 8-day course, but it did not occur if the plasmoquine was discontinued on the 5th day. "Benign tertian sometimes fails to react to these drugs." The report contains a note on an outbreak of poisoning which resulted from the use of Paris green as a larvicide. "The routine treatment of 8 water-holes and a weed-covered pool once weekly, maintained over a period of three months, resulted in the illness of 132 persons, representing a large proportion of the native community using the treated water for domestic purposes . . . the strength of the final dust was 1 : 100." *W. F.*

COVELL (G.), BAILY (J. D.) & VIDYA PRASAD. **An Experiment with Paris Green in a Hyperendemic Village in Sind.**—*Records of the Malaria Survey of India.* 1935. June. Vol. 5. No. 2. pp. 131–152. [11 refs.]

Paris green is not a suitable larvicide for dealing with running water. The control of malaria in hyperendemic rural areas in India is not likely to be achieved by antilarval measures. Lack of funds is the greatest obstacle to the control of malaria in rural areas. The antilarval work described here cost about 2½ pence per head per annum, and that is apparently more than would be available for general use. In the Panama Canal zone, GORGAS spent 2 dollars gold per head, per annum, on malaria prevention. The experiment described by the author was carried out in a hyperendemic village in Sind. Anopheline breeding places were dusted with Paris green for a limited period of each year over a period of 4 years. Conditions were considerably altered during the last two years by the institution of new irrigation under the Lloyd Barrage scheme. There was a partial success during the first two years, but this was not maintained. *W. F.*

COVELL (G.). **The Effect of Paris Green Dusting on Rice Crops.**—*Records of the Malaria Survey of India.* 1935. June. Vol. 5. No. 2. pp. 153–157.

The general opinion among malaria workers is that Paris green has no harmful effect upon rice crops. The farmers in many places say that it is beneficial because it destroys the insect pests. The Deputy Director of Agriculture, Orissa Range, Cuttack, states that Paris green is harmful if applied early in the morning when the flowers are open, but if the dusting is done in the afternoon, when the flowers are closed, no harm results. These opinions were obtained by the author from published papers, and as the result of a questionary sent to malariologists in India and other countries. *W. F.*

SYDENSTRICKER (V. P.) & VRYONIS (G. P.). **Vital Staining of Malarial Parasites. A Preliminary Note.**—*Jl. Lab. & Clin. Med.* 1935. July. Vol. 20. No. 10. pp. 1094–1096. With 1 fig.

The authors have found that for the study of malarial parasites vital staining offers certain advantages over the methods usually adopted. Various stains have been investigated but the best results were given by a saturated solution of brilliant cresyl blue in sterile physiological saline. A small drop of this (2 cmm.) is placed on a slide and a cover glass on which a drop of blood has been placed is dropped on to the stain. The preparation is ringed and is ready for

examination at once, as staining of the parasite is almost instantaneous. The parasites remain alive for upwards of 2 hours on the warm stage. The paper describes the attachment of merozoites to the red cell, their movement over the surface of the cell before penetration, which is followed by the development of an extraparasitic vacuole, and the character of other stages both for *P. vivax* and *P. falciparum*. Changes in the parasites are brought about by the administration of quinine. It seems that the method will be useful for the study of the relation of the parasite to the reticulocyte and of the action of drugs. A black and white half-tone plate illustrates some of the appearances noted.

C. M. Wenyon.

PAWAN (J. L.). **The Preservation in the Tropics of Blood Smears stained by the Romanowsky Stain.**—*Ann. Trop. Med. & Parasit.* 1935. Oct. 5. Vol. 29. No. 3. pp. 327–328.

Seven years ago the author published a note to the effect that Romanowsky stain and its modifications could be kept without deterioration in the tropics if maintained in solution in a Pyrex bottle [this *Bulletin*, 1929, Vol. 26, p. 563]. The preservation of the stained blood smears for future reference or study is another question altogether; they usually deteriorate markedly within a year under tropical conditions. Dr. Pawan finds, however, that if the stained slide be dipped in saturated solution of paraffin wax in xylol (kept saturated at 37·5°C. in the thermostat so that a cloud of solidifying paraffin begins to appear after removal to room temperature), by evaporation of the xylol the slide is coated with a thin layer of paraffin. It can then be put away, and when the slide is needed for examination the paraffin is removed by immersion in xylol. When finished with, the immersion oil is removed with xylol and the whole slide redipped. Thus treated, slides have kept the original staining unaffected for over 5 years in Trinidad, even though exposed to sunlight in the laboratory.

H. H. S.

BOYD (Mark F.). **The Comparative Morphology of the Sporozoites of the Human Species of *Plasmodium*, Marchiafava and Celli, 1885.** —*Jl. Parasitology.* 1935. Aug. Vol. 21. No. 4. pp. 255–259. With 3 plates.

Comparing the sporozoites of the three common malarial parasites of man the author finds that individual variations are so great that species identification is quite unreliable. Nevertheless he finds that generally those of *Plasmodium falciparum* are the finest and those of *P. malariae* the coarsest. Similarly the chromatin mass is densest in the former and most diffuse in the latter. Three pages of outline drawings illustrate the various types of sporozoite observed.

C. M. W.

DE BUCK (A.). Ein morphologischer Unterschied zwischen zwei Plasmodium vivax-Stämmen. [**Difference between Two Strains of *Plasmodium vivax*.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Aug. Vol. 39. No. 8. pp. 342–345. With 1 fig.

Investigating different strains of *Plasmodium vivax* used in the treatment of general paralytics the author finds that the strains differ

from one another as regards the average incubation period, number of parasites present and number of merozoites produced per schizont. These and other differences seem to be present, regardless of the method of infection, whether by inoculation of blood or by the bite of a mosquito, so that they can be regarded as due to inherent characteristics of the strains in question. *C. M. W.*

JAMES (S. P.). Le paludisme par *Plasmodium ovale.* [*Plasmodium ovale.*]—*Riv. di Malariologia.* Sez. II. 1935. Vol. 14. Supp. to No. 3. pp. 27–31.

It is useless to look for *P. ovale* in thick films. It is best to employ two thin ones; one deeply stained to show the changes in the corpuscles, and the other lightly stained to show the character of the pigment and the morphology of the parasite. It is most important to have at hand typical stained specimens of the different species of malaria parasites for comparison; the comparison should be made with the help of a micrometer-eyepiece. It is almost impossible to identify *P. ovale* in the early ring form; in the half-developed stage and later, it looks like a quartan parasite in an hypertrophied corpuscle spotted with Schüffner's dots. Comparison with a type specimen of quartan shows that there are differences in the pigment. An important point is the scalloped or fringed edge of the corpuscle. In the early stages of division, the parasite is rounded and lies in the middle of a large oval corpuscle which is sometimes fringed. The stage of complete division is represented by 8 merozoites, surrounding a central block of pigment, lying in a corpuscle full of Schüffner's dots. (See this *Bulletin*, 1935, Vol. 32, p. 737.) *W. F.*

CHANG (Y. H.), LI (C. C.) & YOUNG (M. P.). **A Clinical and Laboratory Study of 196 Cases of Malaria.**—*Chinese Med. Jl.* 1935. May. Vol. 49. No. 5. pp. 477–478.

This study is based upon 196 cases of malaria in the Elizabeth Blake Hospital, Soochow. Subtertian, 63 per cent., was the most common. Liver damage was shown by the inability to store glycogen, as indicated by the high blood-sugar index 2 hours after a test meal. Albuminuria occurred in 20 per cent. of the subtertian cases and in 6 per cent. of the tertian cases. The case mortality was 1·5 per cent.

W. F.

UTTLEY (K. H.). **A Spleen Rate Survey in the Colony of Hongkong.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. July 31. Vol. 29. No. 2. pp. 187–190.

BOURGIN (P.) & NGUYEN-VAN-TAN. Premier essai sur le paludisme à Soc-trang.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. Feb.–Mar. Vol. 13. No. 2. pp. 97–112. With 5 charts (1 folding).

DALEAS (P.). Paludisme et grossesse. De leur influence réciproque. [**Malaria and Pregnancy.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. May. Vol. 13. No. 4. pp. 432–435.

Parturition and abortion during the course of severe, acute or chronic, insufficiently treated malaria may be followed by collapse. Contrary to common belief, parturition rarely brings on an attack in

cases of latent malaria. The author has found that Henry's reaction is often positive in the newly-born children of Indo-China, and he concludes that congenital malaria is common though parasites are rarely found in the peripheral blood of the babies. *W. F.*

WICKRAMASURIYA (G. A. W.). **Some Observations on Malaria occurring in Association with Pregnancy. With Special Reference to the Transplacental Passage of Parasites from the Maternal to the Foetal Circulation.**—*Jl. Obstet. & Gynaecol. Brit. Empire.* 1935. Oct. Vol. 42. No. 5. pp. 816–834. [14 refs.]

Six cases of congenital malaria are reported: (1) Massive infection of placenta with subtertian parasites. A few parasites in blood from umbilical cord. Baby had rise of temperature on fifth day, but the blood was not re-examined. (2) Massive subtertian infection of placenta; intra-uterine death of foetus; parasites found in foetal brain and spleen. (3) Placental infection, intra-uterine death of foetus; parasites in foetal brain and spleen. (4) Mother died from subtertian malaria; malarial pigment, but no parasites, found in foetus. (5) Mother died from cerebral malaria; subtertian parasites found in heart's blood, spleen and liver of child. (6) Mother died of malaria; crescents found in blood from cord, but none in foetal liver or spleen. *W. F.*

VAN NITSEN (René). Le paludisme chez l'enfant indigène.—*Ann. Soc. Belge de Méd. Trop.* 1935. June 30. Vol. 15. No. 2. pp. 229–268. [13 refs.]

MILNE (J. Coutts). Malaria: Fresh Infections *versus* Relapses.—*Malayan Med. Jl.* 1935. June. Vol. 10. No. 2. pp. 49–50.

ZAUN (F.). Das Verhalten der Leber bei Malaria. (Eine zusammenfassende Uebersicht mit Untersuchungen.) [**The Liver Functions in Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Sept. Vol. 39. No. 9. pp. 363–373. With 3 figs. [67 refs.]

A study of certain functional liver tests in cases of malaria. Attention was directed to the following:—I. Bloodsugar level. 2. The non-protein nitrogen of the blood. 3. The serumbilirubin; and 4. The excretion of urobilin, including urobilinogen. The author summarizes the work which has been done on these subjects including his own. He considers that in malaria a rise in level of the blood sugar suggests an indirect, general damage of an infectious-toxic nature to the liver, the finding of serumbilirubin and urobilin indicates a slow mechanical and chemical damage, a rise of the non-protein nitrogen appears to be related to an increased protein destruction in the body. He considers, however, that further investigations are required to clarify the position. He states that he finds, contrary to some other investigators, that the new drugs, atebrin and plasmoquine, cause no damage to liver function. *E. D. W. Greig.*

TRENSZ (F.). Sur les propriétés antigènes de l'hémozoïne. [**Henry's Reaction. The Antigenic Properties of Haemozöin.**]—*Bull. Soc. Path. Exot.* 1935. July 10. Vol. 28. No. 7. pp. 558–560.

It has no antigenic power.

Henry ascribes his reaction to the presence of antibodies in the blood of malaria patients, which have resulted from the presence of

malaria pigment (haemozoin) which has acted as an antigen in the body. Henry employs melanin as the antigen in his reaction instead of haemozoin, although they are chemically distinct from one another. If Henry's reaction is, as he claims, a specific reaction between antigen and antibody, haemozoin should act even better than melanin. The author obtained haemozoin from the liver and spleen of a fatal case of malaria. It did not give such good results as melanin when it was used in Henry's reaction. Numbers of rabbits were inoculated with haemozoin in order to determine if antibodies were produced. The serum of these rabbits did not floculate with the antigen, nor did the intradermal reaction following the inoculation of haemozoin differ in any way from that in normal rabbits. The author concludes that haemozoin does not act as an antigen. *W. F.*

PRUDHOMME (R. C.). Différents indicateurs remplaçant la mélanine dans la réaction de Henry. [**Henry's Reactions. Substitutes for Melanin as Indicators.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 25. pp. 1115–1117.

The serum of malaria patients has no specific affinity for melanin which merely serves as an indicator of the instability of the serum in distilled water. Many other substances can be used with advantage in place of melanin, and the author recommends a fine suspension of carmine in distilled water. *W. F.*

TRENSZ (E.). De l'emploi d'une mélanine choroidienne purifiée dans la sérofloculation palustre.—*Ann. Inst. Pasteur.* 1935. Aug. Vol. 55. No. 2. pp. 208–226. With 1 chart. [15 refs.]

CHORINE (V.). Floculation et surfloculation dans la réaction de Henry.—*C. R. Soc. Biol.* 1935. Vol. 119. No. 27. pp. 1323–1326.

BRITISH MEDICAL JOURNAL. 1935. Sept. 21. p. 552. **Malaria and its Treatment.**

Colonel JAMES, in opening a discussion at a meeting of the Chemistry Section of the British Association on September 9th, stated that although we disbursed annually nearly £500,000 on the purchase of quinine, yet our expenditure for malarial research amounted to barely a two-hundredth part of this sum. In Ceylon recently, £20,000 was spent on the German drug, atebrin. In this country, he said, there was a backwardness in research into the chemistry of antimalarial drugs. Professor R. ROBINSON stated that the research in England had now reached a stage where further progress was impossible without better facilities. Chemical and biological co-operation was necessary, and a national institute for research in chemical therapy was needed, where chemists and biologists could work together. Professor SCHULEMANN said that he attributed the German successes with atebrin and plasmoquine to co-operation with biologists, and to the new animal tests devised by them. [It is generally accepted that atebrin and plasmoquine are much more likely to cause abdominal pain when they are given together, than when they are given one after the other, and in this discussion, an authoritative statement was made by Professor Schulemann to the effect that this is actually the case.]

W. F.

SOESILO (R.) & GILBERT (A. Ph. W.). Waarnemingen over chemische prophylaxis in een ernstig chronischendemisch malariagebied. [**Prophylactic Drug Treatment in a Hyperendemic Malarial Region.**] —*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. July 8. Vol. 75. No. 14. pp. 1141–1145.

This trial of various remedies was made in the field on an alternate case basis. The total number of children involved was 175 of whom 40 were under and 135 over 3 years; their spleen index amounted to 100 per cent., while the parasite index was 65·7 per cent. All the children received malaria tablets D.V.G. (each containing 240 mgm. quinine sulphate and 2 mgm. plasmoquin) for one week in therapeutic doses, after which the prophylactic trial began of the different test medicaments for a period of 15 weeks: then came stoppage of the medication with continuance of examination of the parasite index, for 28 weeks in all. The groups, I, II, III, IV, with 43, 44, 43, and 45 children in each, received during their course of prophylactic (subtherapeutic) dosage on 3 days in the week ½–1 tablet (50 mgm.) atebrin, ½–2 tablets (100 mgm.) quinine hydrochlorate, ½–2 malaria tablets D.V.G. and anti-beriberi-vitamin tablets respectively. The last group was the control group of no antimalaria treatment. Table A gives the results of the first week of therapeutic treatment and the following 15 weeks of prophylactic treatment. It shows that:— (1) The administration of daily therapeutic doses of D.V.G. malaria tablets for 1 week had lowered the total parasitic index of 65·7 per cent. to 4·5 per cent. (2) The children of atebrin group I remained wholly parasite free. (3) Groups II (quinine) and III (D.V.G.) were never completely free of parasites, but had a much lower parasite index over the whole 15 weeks than before treatment was begun. (4) Control group IV (no treatment) had a consistently higher index than groups II and III, but this was, nevertheless, lower than before the trial began. This lowering is ascribed to lessened chance of infection from the children of the other groups. (5) The great difference between the parasite index of the groups before therapy and during prophylaxis (not higher than 22·8 per cent.) is ascribable to the action of the different preparations, especially as the index in a neighbouring village at the end of the 12th week was 65·2 per cent. (6) D.V.G. malaria tablets in the doses given had less effect than quinine hydrochloride. Table B shows that the stoppage of the prophylaxis resulted in a rise of the parasite index in all the test groups and that the continued action of atebrin for at least 2 weeks is not clearly proven. [D.V.G. apparently stands for *D*ienst der *V*olksgezondheid, and signifies the official malaria tablet.]

W. F. Harvey.

BONNE (W. M.) & STOKER (W. J.). Prophylaxe bij malaria (atebrine, chinoplasmine en chinine). [**Malaria Prophylaxis with Atebrin, Quinoplasmine and Quinine.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. June 11. Vol. 75. No. 12. pp. 958–969. With 1 chart. English summary.

All these drugs acted well as long as they were continued. When they were stopped, there was more malaria than in the untreated control group. Possible danger of acridine sensitization.

The experiments were made in the prison at Bangoredjo, Java. The prisoners were divided into four groups of 75 persons. The first group received one tablet of atebrin (0·1 gram) every evening; the second group, one tablet of quinoplasmine (0·01 gram plasmoquine and 0·3 gram, or 4½ grains, of quinine); the third group, two tablets of quinine (0·4 gram or 6 grains); the fourth group was the control. The drugs were given for three months, and this was followed by an observation period of two months. The results were as follows:—*Atebrin group*: no clinical case of malaria occurred during the three months. Parasites were found only twice at the weekly thick-film blood examination. Three weeks after the treatment had been stopped, the parasite index was no better than in the control group. There were no toxic symptoms, but, at the end of the treatment, every patient was stained yellow. This is objectionable from the standpoint of the patient, it also raises the question of the cumulation of atebrin, and the danger of hypersensitivity to the sun following the deposition of acridine in the skin. The van den Bergh reaction was negative, but positive reactions for urobilin in the urine were more numerous than in other groups. The *quinoplasmine group*: there were two clinical cases, with 44 hospital days. The *quinine group*: there were 4 malaria cases, with 50 hospital days. The *control group*: 21 cases, with 243 hospital days. After the prophylaxis was finished the parasite index, especially in the quinine group, rose abnormally; probably as the result of many latent infections. *W. F.*

DRUMMOND (R.). **Prophylactic Quinine in Malaria in Nyasaland.**—*South African Med. Jl.* 1935. June 22. Vol. 9. No. 12. p. 417.

MARAÑON (Joaquin), PEREZ (Amando) & RUSSELL (Paul F.). **Philippine Totaquina.**—*Philippine Jl. Sci.* 1935. Mar. Vol. 56. No. 3. pp. 229–255. With 2 folding figs. [22 refs.]

Cinchona with an excellent alkaloidal content can be cultivated in the Philippines, and a satisfactory totaquina can be prepared locally and sold at a seventh of the present price of quinine.

The authors have made clinical tests with totaquina extracted at the Bureau of Science from the bark of cinchona trees grown by the Bureau of Forestry in Bukidnow, Miridanao. The plantation was begun in 1927 with seeds obtained from Java, and there are now 38,000 trees consisting of *C. Ledgeriana*, *C. succirubra* and *C. hybrida*, on an area of some 35 acres, situated at an altitude of 2,500 feet, with an annual rainfall of 112 inches and a temperature ranging from 62° to 84°F. Some bark from 5-year-old trees has been analysed with very satisfactory results. The percentage of alkaloids in the *C. Ledgeriana* bark was 9·6 per cent. as compared with 8·52 for India and 8·6 for Java. The yield for *C. hybrida* and *C. succirubra* was about 4·6 per cent. as compared with 6·25 and 7·7 per cent. for *C. succirubra* in India and Java, respectively.

The authors estimate that at least two million cases of malaria occur yearly in the Philippines, and that 32,400 kilograms of quinine are needed on the basis of 250 grains per case per year. The amount of quinine actually imported is often less than 2,000 kilograms a year, because the natives cannot afford to buy it.

"Refined quinine is, in fact, an expensive luxury, a rich man's remedy . . . Therefore, there is a very large field for the production of a still lower-priced product, such as totaquina . . . there is a potential market in the

Philippines alone for more than 30,000 kilograms a year. . . . It is required by malarious consumers who literally cannot afford to buy higher-priced drugs. . . . This estimated retail price of 20·43 pesos per kilogram of totaquina is higher than it would be if production were carried on commercially, but it compares very favorably with the present retail price of 154 pesos for quinine sulphate . . the totaquina could be sold to the people for something like one-seventh of the present price of quinine! In this case a 250-grain treatment would cost not 2·50 pesos, as at present, but only about 35 centavos, a price within the means of the malarious poor."

Successful clinical trials were made by the authors at the Iwahig Penal Colony Hospital with totaquina prepared locally from *Ledgeriana* bark grown in the islands. *W. F.*

SERGENT (André) & VOGT (P.). Essais thérapeutiques du "Totaquina" effectués à l'hôpital de Marengo (Alger).—*Arch. Inst. Pasteur d'Algérie.* 1935. June. Vol. 13. No. 2. pp. 205–209. With 2 figs.

SAINTE-MARIE (Flye). Essais thérapeutiques du "Totaquina" effectués à l'hôpital Cocard, à Fez (Maroc).—*Arch. Inst. Pasteur d'Algérie.* 1935. June. Vol. 13. No. 2. pp. 210-215. With 5 figs.

PETER (F. M.). **The Clinical Testing of Malarial Remedies.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. June 29. Vol. 29. No. 1. pp. 41–50. With 2 charts. [23 refs.]

The author's original observations, made in 1930, have been confirmed by experience.

The author was the first to test atebrin clinically; this he did at the Malaria Research Station, Gurbanesti, Rumania, in 1930 [this *Bulletin*, 1932, Vol. 29, p. 705]. "The present paper aims at showing how far these preliminary clinical tests on a few patients provided correct data regarding the scope of action of this drug." For the purposes of the original test two patients with benign tertian malaria and two with subtertian malaria contracted naturally were chosen, and also a third case of benign tertian which had been infected by inoculation. Films were made every three hours, and the parasites were counted against leucocytes. The observations concerning the action and non-toxic nature of atebrin which the author made in the course of these investigations have been abundantly confirmed in all parts of the world. "It differs fundamentally from quinine and plasmoquine in its longer retention in the body . . . Atebrin is a dyestuff, and its action on the parasites is in all probability a direct one." Atebrin has a marked affinity for the parasites to which it becomes very firmly bound; on this account the amount required should be regulated by the number of parasites present rather than by the weight of the patient. Metabolism of the drug also plays a part in its action, and this can vary even in the same patient at different times. It was observed in the experimental laboratories at Elberfeld, some years ago, that foodstuffs containing large quantities of cellulose absorbed atebrin, and diminished its therapeutic effect. Quantities of milk in the stomach are also said to hinder absorption. As regards individual prophylaxis: unlike quinine and plasmoquine, atebrin prolongs the incubation period, and 0·2 gram on 3 days of each week, or doses of 0·05 to 0·1 gm. daily, will give an effective clinical prophylaxis. *W. F.*

CARMAN (J. A.). **Atebrin, Plasmoquine and Quinine in the Treatment of Malaria.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. July 31. Vol. 29. No. 2. pp. 191–202.

Subtertian infections should be treated immediately; it is vain to hope for the development of immunity against it in European cases. Atebrin is as effective as quinine, and costs no more.

The author states that the primary object of this investigation was to ascertain the relative merits of atebrin and quinine in the treatment of malaria in Kenya, but a large part of his paper deals with the importance of treating cases of subtertian infections as early as possible. In the third General Report of the Malaria Commission of the League of Nations (this *Bulletin*, 1933, Vol. 30, p. 837), it was stated that it is bad practice to begin the treatment of malaria infection at the commencement of the attack since this tends to prevent the development of an acquired immunity (see SINTON & HARBHAGWAN above). The author considers that it is dangerous to postpone treatment, and that to wait for a patient to develop immunity is to risk his life. He does not believe that Europeans ever develop a useful immunity to subtertian malaria. As regards the parallel series of cases treated with different drugs, he found that quinine and atebrin were equally efficient in eliminating parasites. "Atebrin is cheaper in European practice than is quinine, and although in treating Africans in hospital it appears to be less economical to use atebrin, it would almost certainly prove to be cheaper in the long run and in any case its use would enable a given number of beds to be utilised by 14 per cent. more patients."

[Most medical men in the tropics will agree that the treatment of subtertian malaria should begin at the earliest moment, but with regard to the report of the Malaria Commission it should be remembered that it dealt with the subject "from the point of view of persons who are in a position to obtain expert medical advice and efficient care rather than from that of the mass of the population of malarious countries."] *W. F.*

FARINAUD (E.). L'emploi de l'atébrine dans la prophylaxie collective du paludisme dans les exploitations agricoles.—*Ann. de Méd et de Pharm. Colon.* 1935. Jan.–Feb.–Mar. Vol. 33. No. 1. pp. 136–139. With 1 chart.

DE LANGEN (C. D.) & STORM (C. J.). A Comparative Clinical and Experimental Study of the Action of Quinine, Plasmoquine and Atebrin.—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1935. Vol. 24. No. 2. pp. 27–56. [31 refs.]

SOMASUNDRAM (S.). **Temperature Charts illustrating the Action of Atebrin Musonate Intramuscularly compared with Quinine Bihydrochloride Intramuscularly in the Treatment of Malaria in Ceylon.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. July 31. Vol. 29. No. 2. pp. 103–104.

The therapeutic effects of the two drugs were approximately the same. Toxic effects of atebrin by the mouth are not uncommon.

A single injection of 0·375 gram of atebrin was found insufficient to control the disease, and a standard treatment of two intramuscular injections with an interval of 24 hours has been adopted. Occasionally

it has been found necessary to give three injections. The fever and parasites disappear within 3 days. A control series was given two intramuscular injections of 15 grains of quinine followed by 22½ grains a day by the mouth. The author states that he has not found atebrin musonate in any way superior to quinine. Atebrin injections are painless while quinine injections are painful. Atebrin by the mouth frequently causes epigastric pain ; in children it may cause diarrhoea and vomiting. Symptoms of mental derangement lasting 2 or 3 days occurred in a " fair number " of the author's cases towards the end, or after the completion, of treatment. *W. F.*

VAN SLYPE (W.). Résultats cliniques obtenus par les atébrines dans le traitement du paludisme. [**Atebrin in Malaria.**]—*Bruxelles-Méd.* 1935. July 14. Vol. 15. No. 37. pp. 1003–1009.

Atebrin-musonate did not give very good results.

The author treated 54 patients with atebrin and he complains that he had to stop the treatment on several occasions because of vomiting and abdominal pains. [It appears more probable that these toxic symptoms were really due to the plasmoquine which was given with the atebrin.] In one case haemoglobinuria appeared after 0·9 gram of atebrin and 0·09 gram of plasmoquine had been given in three days. The atebrin was given in three forms (1) atebrin tablets, (2) atebrin powder for injection intravenously or intramuscularly, (3) atebrin musonate. A 10-centigram dose of atebrin powder dissolves readily in 5 cc. of water ; it acts promptly ; it is painless when injected and non-toxic. Atebrin musonate is still more soluble, 12·5 centigrams are soluble in 3 cc. of water. It is much slower in its action than ordinary atebrin. In some of the cases treated, schizonts were still present after 10 days. The author recommends that it should be reserved for the treatment of chronic cases. *W. F.*

HICKS (E. P.). **Atebrin Musonate : a Note on the Rate of Absorption and on the Local Effects of Intramuscular Injection.**—*Records of the Malaria Survey of India.* 1935. June. Vol. 5. No. 2. pp. 203–206. [11 refs.]

"A single dose of atebrin musonate was found to have no injurious action on the tissues of monkeys when injected intramuscularly in the strength recommended by the makers."

Atebrin musonate is the methyl sulphonic acid salt of atebrin. Ordinary atebrin is the dihydrochloride. Atebrin musonate is sold as "Atebrin for injection " and must be distinguished from "Atebrin Tablets for Injection " which consist of the dihydrochloride. Atebrin musonate, a yellow powder, is packed in ampullae labelled 0·1 and 0·3 gram respectively. These figures represent the content in terms of the more familiar atebrin dihydrochloride. The actual weights of atebrin musonate are 0·125 and 0·375 gram. The makers recommend that one of the smaller ampoules should be used for intravenous injection, and one to three for intramuscular injection.

BLAZE and SIMEONS (this *Bulletin*, 1935, Vol. 32, p. 746) stated that they could control malaria by the intramuscular injection of one of the larger ampoules on each of two consecutive days. The author's experiments were made with *Silenus rhesus*. The drug was given by intramuscular injection to 8 monkeys, by intravenous injection to 4,

and by the mouth to 4. It appeared to be absorbed more quickly when it was injected. None of the monkeys showed any reaction at the site of injection except in one case where the solution was three times the strength recommended by the makers; in this instance local congestion, haemorrhage and oedema occurred. *W. F.*

AMY (A. C.). **Atebrin and Malaria.** [Correspondence.]—*Jl. Roy. Army Med. Corps.* 1935. Sept. Vol. 65. No. 3. pp. 212–215.

This letter is a criticism of a report on 4 cases of benign tertian which relapsed after treatment with atebrin (see BIGGAM, this *Bulletin*, 1935, Vol. 32, p. 745).

The author quotes a communication issued by Army Headquarters, India, on June 25th, 1934, on the results of atebrin-plasmoquine treatment from April 1st, 1933. Among 1,603 cases of benign tertian malaria 13·6 per cent. relapsed; among 628 cases of subtertian malaria 11·3 per cent. relapsed. A considerable proportion of these were doubtless fresh infections. Atebrin 0·3 gram daily was given for 5 or 7 days, and, then plasmoquine 0·03 gram for a further 5 days. In the case of Indian troops, subsequent to September 1933, the dose of plasmoquine was reduced to 0·02 gram and 0·01 gram on alternate days. The results with a 7-day course of atebrin were slightly better than with a 5-day course. In Bangalore, where there is no possibility of re-infection, 112 cases were treated and none of them relapsed within a period of 2 years. In the Annual Report of the Medical Transactions, 1934, Indian Military Hospital, Quetta, it was stated that all cases of malaria were treated with atebrin and plasmoquine, and that the relapse rate was only 2 per cent. There is absolutely no proof, the author says, that atebrin increases the toxicity of plasmoquine. [See reference above to Schulemann's statement at meeting of British Association.] *W. F.*

DE NUNNO (Renato). La stimolazione antimoniale del s.r.e. come mezzo terapeutico nella malaria estivo-autunnale chinino-plasmochina-atebrin resistente. Nota preventiva. [**Antimony in the Treatment of Resistant Malaria.**]—*Riforma Med.* 1935. July 20. Vol. 51. No. 29. pp. 1087–1092. With 9 figs.

The author employed antimony injections with a view to stimulating the reticulo-endothelial system in patients suffering from malaria infection which had proved refractory to treatment by quinine, plasmoquine and atebrin.

He found that the intravenous injection of antimony tartrate markedly stimulated the r.e. system in rabbits and then tried this drug in cases of human malaria. Details of four are given. He used a 1 per cent. solution in doubly distilled water, sterilizing by heating to 100°C. for half an hour on three days. He gives on alternate days doses of 1, 2, 4, 6, 8, 10, 12 and 14 cc. Sometimes, if signs of intolerance of the larger doses appear, the advance from 9 cc. is more gradual, 10, 10, 11, 11, 12, 12, 13, 13, 14 cc. on alternate days. The early doses often bring about "a true mobilization of the parasites" with febrile attacks, but after the fourth or fifth injection the spleen becomes rapidly smaller and by the end of the course has become normal. One patient was unable to tolerate the complete course of antimony, but after he had received a total amount of 162·5 cgm. of the antimony

salt plasmoquin co. brought about a cure within 3 weeks. If the first course is not sufficient, a second starting at 10 cc. is given after 10–20 days' interval. *H. H. S.*

HUFF (Clay G.). **Natural Immunity and Susceptibility of Culicine Mosquitoes to Avian Malaria.**—*Amer. Jl. Trop. Med.* 1935. July. Vol. 15. No. 4. pp. 427–434. With 1 fig. [12 refs.]

In this paper the author refers to his observations on the susceptibility of culex mosquitoes to infection with bird malaria which have shown that races derived from mosquitoes of low susceptibility tend to contain individuals of low susceptibility, while those derived from individuals of high susceptibility tend to contain individuals which are highly susceptible (this *Bulletin*, 1932, Vol. 29, p. 126). It is also pointed out that as the malarial parasite itself is bisexual the possibilities of the development of variations in it have also to be taken into account when considering the development in mosquitoes and other features of its life-history. *C. M. Wenyon.*

MANWELL (Reginald D.). **How many Species of Avian Malaria Parasites are there?**—*Amer. Jl. Trop. Med.* 1935. May. Vol. 15. No. 3. pp. 265–282. With 49 figs. on 2 plates. [33 refs.]

This paper, which is in many respects similar to a previous one on the same subject by GIOVANNOLA (this *Bulletin*, 1935, Vol. 32, p. 122), reviews the present position of knowledge regarding species of avian malarial parasites. The conclusion reached is that though there may actually be more than seven species only this number have been sufficiently studied to make their existence as separate species certain. These fall into two groups, forms with rounded gametocytes (*P. cathemerium* and *P. praecox* (*relictum*)) and forms with elongate gametocytes (*P. circumflexum*, *P. elongatum*, *P. nucleophilum*, *P. rouxi* and *P. vaughani*). It is probable that *P. capistrani* and *P. wasielewski*, with round gametocytes, and *P. polare* with elongate gametocytes are also good species, while the specificity is questionable, owing to incomplete description, in the case of *P. biziurae*, *P. fallax*, *P. major*, *P. majoris*, and *P. tumbayensis*. The paper contains a great deal of detailed information, while the synonymy of a number of names is discussed. Two of the forms, *P. nucleophilum* and *P. polare*, are new species. Two plates in black and white illustrate the characters of the various parasites. *C. M. W.*

DEMIDOWA (L. W.). Ueber die geringste zur Erzeugung der experimentellen Malaria nötige *Plasmodium praecox* Zahl. I. Mitteilung. [**The Smallest Number of** *Plasmodium praecox* **necessary to give rise to Malaria experimentally.**]—*Giorn. d. Batter. e Immunol.* 1934. Nov. Vol. 13. No. 5. pp. 872–877. [19 refs.] English summary (4 lines).

By means of the micromanipulation and dark field observation of the blood corpuscles the author has been able to inject known numbers of malaria-infected red blood corpuscles into birds. With 50 corpuscles infected with *Plasmodium praecox* 20 birds were inoculated, with development of infection in 5 after 11 to 20 days. With 25 infected corpuscles 40 birds were inoculated, resulting in infection in 3 after

10 to 19 days. With 10 infected corpuscles 45 were inoculated, followed by infection in 2 after 11 to 21 days. With 5 corpuscles 30 were inoculated, followed by infection in 2 after 15 and 16 days. Finally 70 birds received only a single infected corpuscle, resulting in infection in 2 after 14 and 52 days. In another experiment 4 birds received a single corpuscle infected with *P. cathemerium*. Of these one became infected after 5 days. The experiments with *P. praecox* show that by reducing the dose of infective material the normal incubation period of 5–7 days became prolonged to 10–52 days. It is admitted that in these experiments each infected cell may have contained more than one parasite, as it is not possible to distinguish multiple infections from single ones by means of the dark field microscope. *C. M. W.*

LEGROUX (R.) & LWOFF (André). La schizogonie régressive des gamétocytes femelles d'*Haemoproteus paddae*. [**Regressive Schizogony of the Female Gametocyte of** *H. paddae*.]—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. p. 277.

In 1924 the authors saw appearances in *Haemoproteus paddae* of the Java sparrow which they interpreted as the much disputed schizogony of the female gametocyte. Subsequently the discovery of *Plasmodium paddae* in the same host suggested to BRUMPT (this *Bulletin*, 1935, Vol. 32, p. 659) that the forms of the *H. paddae* resembling schizogony were actually schizonts of *P. paddae*. The authors now refute this suggestion, though they rightly point out that experimental work alone will finally settle the question. *C. M. W.*

COATNEY (G. Robert). **The Effect of Atebrin and Plasmochin on the Haemoproteus Infection of the Pigeon.**—*Amer. Jl. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 249–259.

Both atebrin and plasmoquine were tested on *Haemoproteus columbae* of the pigeon the infections employed being the primary ones contracted naturally in the dove-cote. The tolerated doses of the drugs given orally were 40 mgm. of atebrin and 10 mgm. of plasmoquine a day. The conclusion reached is that atebrin inhibits the growth of the young gametocytes and prevents their maturation for at least 55 days. Though the adult gametocytes are altered morphologically atebrin removes them with difficulty. On the other hand plasmoquine does not prevent the development of the gametocytes for more than 15 days but rapidly brings about the disappearance of the adult gametocytes. Neither drug appears to have any effect on the schizonts as judged by the regular occurrence of relapses. *C. M. W.*

SINTON (J. A.). **The Malarial Parasites of the Oriental Monkey** *Silenus irus*.—Reprinted from *Current Science*. 1934. Aug. Vol. 3. No. 2. pp. 48–50.

As has been noted in various other papers, the work carried out by Sinton and his colleagues under the Malaria Survey of India has shown that the oriental monkey, *Silenus irus*, is liable to infection with three species of malarial parasite, all of which are easily transmissible to *Silenus rhesus* by blood inoculation. These parasites are *P. knowlesi*, Sinton & Mulligan, 1932 (24-hour cycle), *P. cynomolgi*, Mayer, 1907 (48-hour cycle) and *P. inui*, Halberstadter & Prowazek, 1907 (72-hour cycle). It is noted that pure infections of these are being maintained at the laboratories at Kasauli. *C. M. W.*

GHOSH (B. N.) & SINTON (J. A.). **Quantitative Changes in the Proteins of the Blood Sera of Monkeys infected with Malarial Plasmodia.**—*Records of the Malaria Survey of India.* 1935. June. Vol. 5. No. 2. pp. 173–202. With 6 graphs. [47 refs.]

The authors, after discussing the work of various observers on the subject of the proteid changes which occur in the serum in human malaria, conclude that the results indicate that malarial attacks cause a distinct fall in total blood proteids, which is most marked in the albumin fraction. Though there seems to be some doubt regarding the globulin fraction there is a general consensus of opinion that the globulin albumin ratio is raised. After the attack there is a tendency for the proteids to return to their normal level. In chronic infections the same changes occur but are less marked. In order to gain further insight into the question it was decided to investigate the blood changes in monkey malaria infections caused by *Plasmodium knowlesi*, *P. cynomolgi* and *P. inui*. The general results indicate a close parallel to what has been found in human malaria. It is noteworthy that the changes are more pronounced with the more acute *P. knowlesi* infection than with the other milder ones. The return of the blood to normal after an attack appears to be accelerated by treatment with quinine, atebrin, plasmoquine or stovarsol. It seems that the disturbance is the result of the effect of the infections on the reticulo-endothelial system. *C. M. W.*

GERACITANO (Arturo). Ulteriore contributo allo studio dell'emozoina malarica. [**Further Contribution regarding Malarial Haemozoin.**]—*Riforma Med.* 1935. July 13. Vol. 51. No. 28. pp. 1058, 1061–1062. With 5 figs. [17 refs.]

The author continues his study of the optical and chemical characters of malaria pigment. He shows that in all three forms (not in *P. vivax* infection only), with crossed Nicol prisms near and between the doubly refractile granules there are others optically inactive and he has proved that these consist of the same pigment. Subjection of the pigment to the action of alcohol, peroxide of hydrogen or hydrochloric acid does not change the double refractivity. It is worthy of note, he states, that malarial pigment, which is optically active to polarized light is related to and resembles the haemin crystals of blood. *H. H. S.*

JACKSON (R.). Sur deux cas d'infection naturelle par l'hématozoaire du paludisme, de *A. splendidus* (*A. maculipalpis*) dans la colonie de Hong-Kong. [**The Natural Infection of** *A. splendidus* (*A. maculipalpis*) **in Hong Kong.**]—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 446–448.

The author has found two specimens with gut infections; one with 15 cysts of about 10 μ diameter, the other with 12 measuring about 40 μ. They were caught in a construction camp at Shing-Mun, on the mainland, where the rate of infection of the principal carriers was very high. The figures were as follows:—

A. minimus, examined 2,155, infected 12·48 per cent.; *A. jeyporensis*, examined 10,936, infected 9·93 per cent.; *A. maculatus*, examined 230, infected 3·48 per cent.; *A. hyrcanus*, examined 2,818, infected 1·21 per cent. *W. F.*

MATHIS (Maurice). Cycle biologique complet d'*Anopheles gambiae* Giles élevé en série au laboratoire. [**The Complete Life-Cycle of** *Anopheles gambiae* **realized, in the Laboratory.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 27. pp. 1385–1386.

The author bred *A. gambiae* in small cages measuring only 18 × 18 × 25 centimetres. The water for the larvae was rich in *Protococcus* and was further enriched with a sterile culture of *Euglena viridans*. The eggs hatched in 36 to 40 hours; the larvae became pupae in 5 to 8 days; adults appeared 24 hours later; fecundation took place quite readily in the small cages on the same evening; the females were ready to bite almost at once; the first eggs were deposited about 6 hours after the feed. The whole cycle from egg to egg occupied about a fortnight. The author has successfully carried on a strain of *A. gambiae* at Dakar, in Senegal, through 5 generations, between 29th April and 14th July 1935. The temperature was 24–26°C. This has provided him with several thousand mosquitoes. *W. F.*

BOYD (Mark F.), STRATMAN-THOMAS (Warren K.) & KITCHEN (S. F.). **On the Relative Susceptibility of** *Anopheles quadrimaculatus* **to** *Plasmodium vivax* **and** *Plasmodium falciparum*.—*Amer. Jl. Trop. Med.* 1935. July. Vol. 15. No. 4. pp. 485–493.

When the gametocyte density is high, *Anopheles quadrimaculatus* can be infected in approximately the same degree with either *P. vivax* or *P. falciparum*; but when the gametocyte density is low, infection with *P. vivax* occurs more readily. One male and one female gametocyte to 100 leucocytes marks the nominal practical limit for the infection of *A. quadrimaculatus* with *P. vivax*, but the minimal density in the case of *P. falciparum* is 11 gametocytes of each sex to 100 leucocytes. The authors "incline to the opinion that the differences noted may more properly be attributed to characteristics of the parasites themselves than to a differential susceptibility on the part of *A. quadrimaculatus*." *W. F.*

DE BUCK (A.). **Infection Experiments with Quartan Malaria.**—*Ann. Trop. Med. & Parasit.* 1935. July 17. Vol. 29. No. 2. pp. 171–175. [10 refs.]

A fair percentage of gland infections was obtained with one batch of *A. maculipennis*, the results with other batches were very poor.

These experiments were carried out in Amsterdam with a quartan strain obtained from Vienna. Wild *A. maculipennis* var. *atroparvus* which had been caught in stables were fed on two patients who had been inoculated with this strain. The number of male gametocytes in the blood at the time of feeding was 6 per 500 leucocytes, or somewhat over the density of 1 per 100, which the author considers the minimum concentration for practical use. The result was unexpectedly successful for out of 45 mosquitoes which were dissected 12 showed gland infections. The experiment was repeated several times, but the same good results were not obtained. In one batch, 5 gland infections were found in 56 mosquitoes dissected, but in other batches there were no infections beyond a few oöcysts in the gut. "The only reasonable explanation seems to be that the number of gametocytes in the patient's blood was sufficient, but that the bad results in the

other mosquitoes are caused by something in the physiology of their stomachs." Experiments made with *A. bifurcatus* gave the same bad results. The extrinsic incubation was 15 days, the intrinsic incubation, in man, was 25 days. "The Vienna strain of malaria quartana develops only in rare cases a sufficient number of gametocytes to infect mosquitoes successfully." ***W. F.***

BISHOPP (F. C.). **Mosquito Control Work of To-day.**—*Jl. Econom. Entom.* 1935. June. Vol. 28. No. 3. pp. 620–627.

While passing reference is made to other parts of the world in which effective mosquito control has been carried out, this paper is concerned with what has been done in the United States of America, where in certain areas the problem has been tackled in a wholesale manner under Federal or State supervision and support. Non-malaria-carrying as well as malarial mosquitoes have received attention, the former in 32 States and the District of Columbia, the latter in 14 States. The assumption by the Civil Works Administration in December, 1933, of responsibility under both headings gave a great stimulus to operations, which in "nearly all the Southern States" had already been in progress for a long time. That extensive mosquito control may also afford at least temporary relief to unemployment is shown by the fact that, in the 14 States already mentioned, the monthly average of men employed for some 4 months in ditching and draining was 64,000, while "The maximum number of labourers at work during any week of this period was 120,000."

The author pleads for further research into the bionomics and ecology of mosquitoes, as also their relation to virus diseases, such as encephalomyelitis, in man and animals. *E. E. Austen.*

i. DE BUCK (A.) & SWELLENGREBEL (N. H.). **The Salivary Glands in Hibernating** *Anopheles maculipennis* **var.** *messeae* **and Semi-hibernating** *Anopheles maculipennis* **var.** *atroparvus.*—Reprinted from *Proc. Roy. Acad. Amsterdam.* 1935. Vol. 38. No. 4. pp. 452–454. With 3 figs. on 1 plate.

ii. —— & ——. **Further Studies on, and Discussion of the Results of Crossmating the Races (Varieties) of** *Anopheles maculipennis.* —*Ibid.* No. 5. pp. 553–558. With 6 figs. on 2 plates.

i. In villages to the north of Amsterdam, in attics wherein people sleep, both varieties mentioned in the title occur in autumn and winter, *messeae* because of the lowness of the temperature in such places, *atroparvus* on account of the facilities for feeding. Once there, *messeae* remains fasting, while *atroparvus* takes a meal of blood at intervals. Thus, though the environment is the same, the two varieties behave differently. Examination of the salivary glands affords a means of identification. In *messeae* the glands are typically "rod-shaped," and frequently contain masses of needle-like crystals in the lateral lobes; in typical *atroparvus* the glands are "club-shaped," and devoid of crystals.

ii. In order to check the results described in a previous paper [this *Bulletin*, 1935, Vol. 32, p. 137], the authors repeated their experiments in crossmating the varieties of *A. maculipennis* which occur in Holland, namely *atroparvus*, *messeae* and *typicus*, using adults reared in Amsterdam from ova collected in Sweden. These "responded to

attempts at hybridisation in exactly the same manner as specimens collected in Holland and in Italy." Crossing (both ways) *atroparvus* and *messeae*, and crossing female *atroparvus* with male *typicus* did not result in viable larvae. On the other hand, by crossing male *atroparvus* with female *typicus* there was produced a first filial generation, which was sterile. *E. E. A.*

DE BUCK (A.) & SWELLENGREBEL (N. H.). **On the Seasonal Longevity of *Anopheles maculipennis* in Holland with Reference to their Ability to act as Malarial Vectors.**—Reprinted from *Proc. Roy. Acad. Amsterdam.* 1935. Vol. 38. No. 3. pp. 335–343. With 3 diagrams.

The scarcity of summer infections in anopheles is not due to stabular attraction only, but also to the short life of summer generations. Heavily infected mosquitoes live the shortest time.

JAMES, NICOL & SHUTE have shown that the early summer is not favourable to malaria transmission, because it is not favourable to the longevity of infected anopheles. It is not favourable to their longevity because this is a period of sexual activity which endangers life by ovulation and long flights. It was formerly thought that the difficulty of finding anopheles in houses in Holland during the summer was due to their being attracted to stables; JAMES's observations admit of a different interpretation.

Observations made by the authors gave results which agreed with those of JAMES. "A favourable season from September till December (rate of survival 59 per cent.), an unfavourable one from April till August (rate of survival 15 per cent.), joined by a period of transition in January–March (rate of survival 32 per cent.). The sporozoite rates of anopheles infected within these three periods are about the same, *viz.*, 74, 70 and 71 per cent. respectively. So the summer mosquitoes are indifferent malaria vectors not because they are bad carriers but because they are too short-lived." Except in the winter months laboratory-bred mosquitoes live much longer than wild ones. The latter are weakened by the wear and tear of an outdoor life during the period of sexual activity. This confirms JAMES's views on the special importance as malaria vectors of anopheles protected from the dangers of an outdoor life. The author found " that there exists a greater mortality in heavily infected mosquitoes than in slightly infected ones. Whatever the cause may be of this increased mortality it is acting only during the unfavourable season of February–August and it affects the mosquitoes suffering from a salivary infection. Intestinal infection alone, however severe, does no apparent harm."

W. F.

GALLIARD (H.) & SAUTET (J.). Nouvelle contribution à l'étude de l'anophélisme en Corse. Les variations saisonnières de l'indice maxillaire. [**Anophelism in Corsica : the Seasonal Variations in the Maxillary Index.**]—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 453–456. With 2 figs. on 1 plate.

In Corsica by far the most important vectors of malaria are *Anopheles maculipennis* var. *labranchiae* and *A. sacharovi* (*A. elutus*), which in certain parts of the island exhibit seasonal instability as regards the maxillary index. During the summer, when malaria is epidemic, the

mean maxillary index was found to be between 12 and 14, whereas in winter, in two successive years, it fluctuated between 13 and 16. Such variation would seem to be connected with changes in the breeding places, partly seasonal, partly (in one instance) due to pumping. As already remarked by ROUBAUD, with regard to the race of *A. maculipennis* in Vendée whose zoophily is unstable :—" a rise in the mean maxillary index corresponds to the diminution of water surfaces; conversely, the lowering of the index will be related to a marked extension of the latter. . . ." In September, when breeding places exhibit their maximum reduction before the first rains, competition among larvae is intense, and it is possible that the only individuals to complete their development will be such as are stronger than their fellows; hibernating females thus produced will, according to ROUBAUD's hypothesis, have a high maxillary index. In Holland, on the other hand, according to DE BUCK, SCHOUTE & SWELLENGREBEL, the reverse is the case, and a rise in the maxillary index is observed when the winter generation gives place to that of summer; this difference, however, may be partly climatic, and partly due to the fact that the Dutch races of *A. maculipennis* all have a very high maxillary index, besides contrasting with the southern races in many biological respects. An unstable anopheline fauna, whose reactions, in default of prolonged study, cannot be foreseen, is dangerous. Where such exists in a malarious region, hasty and incomplete interference with water-surfaces may be inadvisable. *E. E. A.*

WASSILIEFF (A.). Étude de quelques gîtes d'anophèles tunisiens. [**Some Breeding Places of Tunisian Anopheles.**]—*Arch. Inst. Pasteur de Tunis.* 1935. Apr. Vol. 24. No. 2. pp. 352–359.

The author has studied and made collections in two permanent Anopheles breeding places in Tunis. In one, part of the Oued Bezirck, the water is fresh, the mosquito is *A. maculipennis*, and its larvae were found in abundance among an aquatic plant community consisting of seven species, the names of which are given. In the other, the Bekalta drains, the water is brackish, the mosquito is *A. hispaniola*, and the plant association consists of only three species, which are different from those in the Oued Bezirck. The single feature common to the two plant communities is that their leaves are finely divided, so that they form a network in the water. In the localities mentioned, the antilarval campaign should concentrate on the eradication of aquatic plants; the suppression of amphibious plants, growing along the edge of the water, is less important, and oiling should follow the uprooting of the others. The finding of larvae of *A. hispaniola* in different stages of development during November and December indicates the advisability, where this mosquito occurs, of not discontinuing antilarval measures even in winter. *E. E. A.*

SERGENT (Etienne). Quelques remarques sur les espaces intercostaux et les columelles des oeufs d'*Anopheles maculipennis*. [**The Intercostal Spaces and the Columellae in the Eggs of** *Anopheles maculipennis*.]—*Arch. Inst. Pasteur d'Algérie.* 1935. June. Vol. 13. No. 2. pp. 184–187. With 17 figs. on 5 plates.

The author has examined, compared and photographed samples from 144 batches of eggs of Algerian *A. maculipennis* var. *labranchiae*, and has similarly studied eggs laid by French representatives of vars.

atroparvus and *messeae*, as furnished by 162 batches produced by the former, and three deposited by the latter, in Limousin and Cantal. The brief paper under review provides a commentary on the excellent, untouched photographs with which it is illustrated. In the determination of the varieties of *A. maculipennis*, HACKETT & MISSIROLI have attached a certain importance to the appearance of the intercostal membrane in the floats on the eggs; and the forms of wrinkling of this membrane exhibited by the varieties mentioned above are displayed in the plates. As is only to be expected, the markings in question do not provide absolutely distinctive characters, and in eggs of var. *atroparvus* the intercostal spaces may be either wrinkled or smooth. On the other hand, photographs of portions of the undersurface of the egg-floats in the same variety and in var. *labranchiae* show a similar kind of network, formed by longitudinal wrinkles. The illustrations of the columellae (or, as the author would prefer to term them, the *papillae*) in the eggs of vars. *labranchiae* and *atroparvus* agree with the descriptions in "Instructions for the Determination of the Varieties of *Anopheles maculipennis*," issued by the Malaria Commission of the League of Nations. *E. E. A.*

i. COLLIGNON (E.). Quelques observations sur le comportement des anophèles dans leurs abris diurnes en Algérie. [**The Behaviour of *Anopheles* in their Diurnal Shelters in Algeria.**]—*Arch. Inst. Pasteur d'Algérie.* 1935. June. Vol. 13. No. 2. pp. 188–191.

ii. ——. Observations sur les gîtes à anophélines dans le département d'Alger en 1934. [**Anopheline Breeding-Places in the Department of Algiers, in 1934.**]—*Ibid.* pp. 192–200. With 1 chart.

i. With the object of testing the effect of antilarval measures, and in order to secure specimens for laboratory purposes, the author, in 1934, paid frequent visits to certain dark cow-sheds in the vicinity of Halloula Lake and Rhégaïa Marsh, important breeding-places of *Anopheles maculipennis*. In these shelters, untenanted by day, the insects were found resting on the underside of roofing tiles, on rafters, or on the upper part of the walls, especially, as so often happens, on dusty cobwebs. Almost all were females, gorged with blood, and eggs subsequently deposited were exclusively of the *labranchiae* type. Males, seen rarely at the beginning of spring, were never met with again, even though the breeding-places were but a few hundred metres away. No *Anopheles* were found among vegetation in the surrounding open country. As in the British Isles, a summer and an autumn brood would appear to be produced; individuals belonging to the former were found from the latter end of May or beginning of June until August, while those of the autumnal series were in occupation of the sheds from the commencement of October until the end of the following month or even of December. At the outset of the hot weather as also in autumn, the insects were found chiefly in the upper parts of the cow-sheds, near the roof; at the end of June, when they were most numerous, they extended on to the walls, but did not descend lower than about 1½ metre from the ground. With a damp sea-breeze from the north-east the shelters were well occupied; on the other hand, when the sirocco, the dry wind from the south, was blowing, it was seldom that even a few insects could be found, and the sheds were deserted for some time afterwards. In June, at the beginning

of the hot weather when the sun was most powerful, captures could be made with ease; but in December the insects seemed more wide-awake, and frequently took flight so soon as a beam of light fell upon them.

ii. The year 1934 in Algeria was marked by an abnormal rainfall, resulting in a considerable extension of permanent Anopheles breeding-places, and an unusual persistence of temporary ones. Details are given with regard to breeding-places of *Anopheles marteri*, *A. bifurcatus*, *A. hispaniola*, *A. maculipennis* and *A. algeriensis*. The early stages of the last-mentioned species had not previously been met with by the author, but in 1934 he took larvae and pupae in two different localities near the seashore.

In the case of *A. maculipennis* breeding began very late, and it was not until the beginning of June that the first larvae were found, the influence of the water régime being shown by the fact that captures were made at about the same time in all districts. Generally speaking, larvae persisted until the end of November, and a breeding place on the seashore, which had formed again in the autumn, still contained larvae at the close of December. In 1934, larvae of *A. maculipennis*, often alone but sometimes associated with those of other species of the genus, were encountered in almost every breeding place examined.

E. E. A.

DE MEILLON (Botha). **Entomological Studies. Studies on Insects of Medical Importance in South Africa—Part II.**—*Publications of South African Inst. Med. Res.* 1935. Mar. Vol. 6. No. 35. pp. 323–365. With 10 plates.

The first portion of this paper is concerned with Simuliidae. There follows, after records of mosquitoes found in the Cape Province, an account of experiments with *Anopheles funestus*, an "essentially anthropophilic" species. When a native in an infested area was made to pass the night in an open-ended, mosquito-proof tent, through which a gentle breeze was caused to blow, 60 *A. funestus* were caught on the gauze protecting the leeward end, but none on that covering the other, showing that the insects found the host by smell. Two further series of similar experiments, each lasting eight days, during which the native was receiving doses of sulphur with the object of disguising his odour, showed that "the ingestion of sulphur, some of which is excreted through the skin, and so presumably disguises the body odour of the host," reduced the number of *A. funestus* which visited the tent in order to feed. When the host, after being carefully deodorized, was sprayed with capryllic alcohol, "apparently an essential feature of goat odour," before being placed in the experimental tent, *A. funestus* ignored his presence for three successive nights; and the simple deodorizing of the host with odourless soap and water, followed by the application of weak hypochlorite solution, proved nearly as effective, the total bag of *A. funestus* on three successive nights being in this case 11 in the experimental as compared with 69 in the control tent. The author's conclusion is that immunity from mosquito bites may possibly be secured either by the application of "some odourless substance" (thus avoiding the use of strong-smelling and to some people objectionable citronella), or by ingestion of something "which, when excreted through the skin, will neutralize the body odours without giving the body an additional smell."

In a brief concluding section anatomical and bionomical reasons are given for thinking that *A. funestus* subsp. *leesoni* is really a distinct species, which on the other hand, as shown by certain adult and larval characters, is also distinct from the Oriental *A. fluviatilis*. *E. E. A.*

i. TREILLARD (M.). Domesticité périodique et périodicité de la pullulation chez les anophèles extrêmes-orientaux. Remarques sur ses modalités, ses causes et son utilisation. [**Periodic Domesticity and Abundance of Far Eastern Anopheles : their Characteristics, Causes and Utilization.**]—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 448–450.

ii. ——. Influence des facteurs externes sur la biologie des larves d'anophèles. I. Surface, volume, profondeur de l'eau et développement des larves de *Pseudomyzomyia subpicta*. [**Influence of External Factors on the Biology of Anopheline Larvae. I. Surface, Volume and Depth of Water, and the Development of Larvae of** *Anopheles subpictus*.]—*Ibid.* pp. 451–452.

i. One of the chief objections likely to be urged against an anti-adult mosquito campaign is that it can only affect a relatively limited number of insects, representing at best a more or less important fraction of the total anopheline population. But, unless hopes are vitiated by wholesale outdoor migratory movements of adult anophelines, it should be possible, by choosing the moment or moments when the numbers of domestic mosquitoes are lowest, to effect what will amount to a large-scale destruction of the anopheline population. In the case of *Anopheles minimus*, which is so formidable a vector of malaria in the Far East, migrations of the character referred to have not yet been demonstrated. In view, therefore, of its domesticity, anthropophily, and individual longevity, and of the duration of the period when it is on the wing, it can be attacked with success indoors while its numbers are relatively low, although, as already pointed out by the author [this *Bulletin*, 1931, Vol. 31, p. 719], owing to the nature of its breeding-places antilarval measures against it may be difficult.

ii. Among the various kinds of breeding places selected by *A. subpictus*, which is fairly widely distributed in the Far East, small household collections of water are most frequently chosen. The author has noted the results of placing twenty young larvae of this species separately in each of four series of small containers, the respective diameters of which were 1·5, 1·5, 9 and 9 cm., and the heights 0·5, 4, 0·5 and 4 cm. Not only the exposed surface and the depth of water thus varied, but also the volume, the latter ranging from some 2 cc. in the smallest receptacles to about 100 cc. in the largest. Other conditions, including temperature and food-supply, were the same throughout. Results, to be published in detail later, are given in concentrated form, and it is noted that the same type of rearing receptacle did not prove equally favourable to both pupae and larvae, either as regards number developing or time occupied. Receptacles belonging to Series I, *i.e.* the smallest, produced the largest number of adults in the shortest time, and were closely followed in this respect by Series III. It would seem that the experimental results described, which show the benefit arising from the disposition of a certain quantity of water, are in accordance with conditions observed fairly often in the natural breeding places of *A. subpictus*. *E. E. A.*

SOESILO (R.). **The Hyrcanus (Sinensis) Problem in Java. (Preliminary Report.)**—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1935. Vol. 24. No. 2. pp. 68–71.

This concerns the important part played by *A. hyrcanus* in an epidemic on the Pamanoelean and Tjrasern lands near Soembang, in Java. WALCH was the first to describe a *hyrcanus* epidemic; it occurred on the east coast of Sumatra in 1921. In some parts of the interior it is the most important carrier. WALCH subjected specimens from various parts of the archipelago to the precipitin test. He found that about 85 per cent. contained human blood and that the presence or absence of cattle made little difference. [See SWELLENGREBEL above, where it is stated that *hyrcanus* is not a carrier in the rice fields of Java, though it is present in great numbers.] *W. F.*

BAISAS (F. E.). Notes on Philippine Mosquitoes, II. Uranotaenia Group. —*Philippine Jl. Sci.* 1935. May. Vol. 57. No. 1. pp. 63–80. With 4 plates & 1 fig. [27 refs.]

BAISAS (F. E.). Notes on Philippine Mosquitoes, III. Genus Culex: Groups Lophoceratomyia, Mochthogenes, and Neoculex.—*Philippine Jl. Sci.* 1935. June. Vol. 57. No. 2. pp. 167–179. With 2 figs. & 4 plates. [20 refs.]

HINGST (Hans E.). A Note on making Permanent Preparations of Anopheline Mid-Guts.—*Amer. Jl. Hyg.* 1935. Sept. Vol. 22. No. 2. pp. 278–282. With 5 figs.

LING (L. C.). **Field Observations on Malaria Control Measures in Singapore and Java.**—*Chinese Med. Jl.* 1935. June. Vol. 49. No. 6. pp. 562–569. With 9 figs.

The antimalaria budget for Singapore Municipality is given, and the method of controlling malaria in the rice fields of Java is described.

With the help of a fellowship given by the League of Nations, the author attended the malaria course arranged by the Health Organization of the League at Singapore in 1934. The course lasted two months; it consisted of laboratory work and practical field study and was attended by 27 students who were divided into two parties, one of which studied field work in Malaya and the other in Java. The author describes his experiences in Singapore and Java. The budget for antimalaria work in the municipal area of Singapore, for the year 1934, was 71,150 Straits dollars (£8,300) of which $43,685 was for coolies' wages, $20,335 for equipment and materials, $7,130 for salaries of inspectors. The municipal area has a radius of 5 miles with a population of about half a million. In Java, the malaria of rice fields is carried by *A. aconitus*; in Sumatra, it is carried by *A. hyrcanus* var. *sinensis*. The incidence of these mosquitoes has been reduced by attention to the grass and the water. The period of irrigation has been shortened; the inlet and outlet of water has been better controlled; the farmers are allowed to plant only one crop of rice instead of two, and that must be done at a fixed time during the wet season; they are made to keep the irrigation ditches free from grass. Free quinine is distributed during epidemics. These measures have achieved remarkable success; in the Tjihea Plain of Western

Java, where rice fields had been abandoned because of their unhealthiness, the spleen index has dropped in 3 years from 100 per cent. to almost nothing, the population has increased by 30 per cent., and a rice of better quality which sells at a higher price has been produced. The author also describes the methods by which breeding in fish ponds is controlled. (See this *Bulletin*, 1935, Vol. 32, p. 729, and 1930, Vol. 27, p. 640.) *W. F.*

GINSBURG (J. M.). **Mosquito Larvicides.**—*Proc. N. J. Mosq. Ext. Assoc.* 1934. p. 121. [Summarized in *Dept. Scient. & Indust. Res. Water Pollution Research. Summary of Current Literature.* 1935. Sept. Vol. 8. No. 9. pp. 297–298.]

"A stable stock emulsion suitable for use as a larvicide in fresh waters and waters of less than 5 per cent. salinity is prepared by emulsifying a mixture of kerosene-pyrethrum extract (obtained by treating 2 lb. pyrethrum flowers with 2 gal. kerosene), 1 gal. water, and 8 oz. 40 per cent. liquid coconut oil soap. The emulsion mixed with 10 parts of water kills mosquito larvae but is not injurious to fish, plants or water fowl. The pyrethrum does not remain toxic after 48 hours. An emulsion suitable for use on waters of more than 5 per cent. salinity is prepared by adding a mixture of 2 oz. cresylic acid and 2 gal. kerosene-pyrethrum extract to a mixture of 1 lb. powdered skim milk in 1 gal. water. Diluted with 10 parts water, this larvicide has no effect on goldfish and water fowl but causes slight injury to young leaves of aquatic plants. Both larvicides are equally effective against mosquito pupae and larvae when used at a rate of 50 gal. or more per acre. On account of insufficient spreading and penetration, the pyrethrum larvicides are less effective than oil on waters covered with vegetation and debris, filter beds heavily charged with sewage and scum, salt water covered with scum and places where the more permanent effect of oil is necessary; under other conditions they are as effective as oil. Soap in a concentration of 0·2 per cent. or more completely destroys mosquito larvae and pupae."

RIMBAUT (G.) & MATHIS (Maurice). Utilisation des "poissons millions" pour la lutte biologique contre les larves d'anophèles à Dakar. [**The Successful Employment of "Millions" at Dakar.**] —*Bull. Soc. Path. Exot.* 1935. July 10. Vol. 28. No. 7. pp. 575–577.

These small fish are native to the northern part of South America and the Lesser Antilles. They are very small, the females measuring only 5 cm., and they are very prolific and bring forth 30 to 60 young every month which themselves attain to maturity a couple of months later. Conditions at Dakar are favourable to these little fish, and three couples brought from the Pasteur Institute in Paris multiplied rapidly. Dakar is surrounded with vegetable gardens containing innumerable wells which, however useful they may be to the market-gardeners, serve as a chain of anopheline breeding-places round the settlement. Ten fish were put into one of these wells, a shallow pool excavated in the sandy soil, and the contents of 10 dips of the net were counted daily. On the first day, there were 1,500 larvae and 10 fish; on the fourth, 604 larvae; on the fifteenth, 205 larvae;

on the twenty-ninth, 0 larvae and about 600 fish. The gardeners welcome the use of "millions" in preference to oiling, and it is cheaper. *W. F.*

DEARBORN (F. E.). **Homologs of Paris Green. I. Lower Members of Acetic Acid Series.**—*Jl. Econom. Entom.* 1935. Aug. Vol. 28. No. 4. pp. 710–714.

Copper aceto-arsenite, or Paris green, has been a commercial product for nearly a century. Its principal use prior to 1870 was as a pigment. It came into wide use for poisoning the Colorado potato-beetle and other insects before the introduction of lead arsenite as an insecticide. In 1906 Avery prepared a series in which formic, proprionic, butyric, monochloracetic and trichloracetic acids were substituted for acetic acid. His conclusions were that Paris green and its homologues were compounds of copper meta-arsenite and the copper salt of the acid used, in which the ratio most frequently approached 3 to 1. The analyses made by the author show that Paris green and its homologues are definite compounds of copper meta-arsenite and the copper salt of the corresponding acid, and that the ratio of the two constituents is very close to 3 : 1 in all cases. *W. F.*

WINCKEL (Ch. W. F.). Die Praxis der therapeutischen Malaria. [**Malarial Therapy.**]—Reprinted from *Psychiatrische en Neurologische Bladen.* 1935. No. 3. 20 pp. With 14 charts. [13 refs.]

An account of malaria therapy as practised in Amsterdam. The author is the malaria consultant to the Psychiatric Clinic at Amsterdam. He gives a clear account of the methods employed there for malaria therapy. These do not differ much from those now generally employed. One or two points may be referred to. In order to damp down the symptoms of the infection when they tend to get out of hand, but not to kill off all the parasites, an injection of a small dose (150 mgm.) of neosalvarsan is recommended. They have now abandoned the use of provocatives or "stimulants" of the malarial infection, adrenalin, etc., as being unnecessary when systematic blood examinations are being carried out. The importance of regular blood examinations is rightly stressed. As the number of cases of general paralysis of the insane is limited in Amsterdam itself he considers that it would improve the organization and facilities for investigation if cases in the north and south province of Holland and Utrecht were included in the scheme. Amsterdam acts as a centre for distributing malarial blood to various clinics in Holland. *E. D. W. Greig.*

REVIEWS AND NOTICES.

McKinley (Earl Baldwin) [M.D., etc.]. **A Geography of Disease. A Preliminary Survey of the Incidence and Distribution of Tropical and Certain Other Diseases.** Supplement to *Amer. Jl. Trop. Med.* 1935. Sept. Vol. 15. No. 5. pp. xxv+495.

This Survey was made possible by a grant from the American Leprosy Foundation to the Division of Medical Sciences of the National Research Council, U.S.A., and is dedicated to the memory of Theobald Smith, who was one of an advisory Committee of three. The author is Director of Studies to the Division. One of the objects is stated to be to give impetus and encouragement to the development of the field of tropical medicine by both lay and professional interests. Statistical data from tropical and subtropical countries in all parts of the world are presented in tabular form, supplemented by sketches of the social-economic background of each area, for which acknowledgment is made to the "Statesmen's Yearbook." These tables and letterpress make up the bulk of the survey. They are followed by short essays on 18 selected diseases, regarded as world problems, by American authorities, with statistical summaries and references and by an Appendix of comments on various subjects from different parts of the world which were unsuited for inclusion in the body of the survey.

A survey such as this might be based on a study of the reports issued by Governments and Institutions or by a questionary circulated to medical departments or individuals in the areas from which information was desired. From many areas, however, reports are not available and when such are issued the differences in their form and method of presentation make comparison difficult if not impossible, and it is the questionary which has been here adopted. This is in two parts: 1. Tropical Diseases. 2. Diseases usually considered as of Temperate Climates. In the first list there are 80 entries, and many of these have sub-heads. The second list contains 32 entries.

Following the column of disease headings are five blank columns, for the presence or absence of the disease, its distribution, number of cases, vector or intermediate host, and whether considered important in public health or not.

No two authorities or even authoritative committees would be likely to agree on the best form of such a questionary and, taking it as it stands, the reviewer ventures to suggest, in the light of the returns, that some definitions or expansion of headings would have cleared up ambiguities.

Some of the disease headings have been variously interpreted. Thus "tropical liver" is by some considered to be amoebiasis of that organ, by others as something else. "Septic sore" may mean ulcers apart from ulcus tropicum, which has its own heading, but that it does not usually convey this meaning is shown by the fact that in some tropical African returns "septic sore" does not figure at all, and chronic ulcers get their only mention in a footnote to ulcus tropicum.

"Tinea imbricata" should not have presented difficulty; it is a well-recognized disease chiefly found in islands of the Pacific; but in several African returns a large number of cases are recorded with the footnote that Tinea is meant [the printer has usually rendered it Taenia]; one must conclude that most of the ringworms appear under

this head. "Climatic bubo" too is a well-defined condition, more appropriately named, now that its nature is known, Poradenitis or Lymphogranuloma inguinale; many cases are returned as such with a note that "non-specific bubo" is meant. It is indeed necessary to study the footnotes in every return.

Would not a transposition of words have improved the heading of the second column, "Present or absent now or previously"? The wording perhaps accounts for the + sign in the yellow fever returns from Uganda, Tanganyika, Zanzibar and Straits Settlements. As the question is worded the reply must under any conditions be "Yes."

It is satisfactory to note that the British Empire portion of the survey occupies 193 pages, against 44 for French possessions and less for other countries; there are no returns from Algeria or Tunis. Dr. McKinley justly acknowledges the help afforded him by SCOTT's Supplements to the *Tropical Diseases Bulletin.*

The survey is a mine of information to the professional man who will not be misled by returns in which presumably sporadic cases are recorded, *e.g.*, St. Lucia, in which kala azar, trypanosomiasis and guinea-worm have the + sign and Gibraltar, in which returns most tropical diseases have a +, the number of cases for the year in question (1932) being in 27 instances recorded as 0.

If it is intended to pursue this enquiry and publish a further volume the recorders might be asked to state in what proportion of diseases caused by animal parasites the diagnosis was made by microscope; in some instances this is stated. In a revised questionary room might be found for Fevers of Unknown Origin and Infective Eye Diseases other than Trachoma.

Dr. McKinley and his collaborators have done a useful piece of work. The inquirer will find here under one cover tables of the diseases recorded in nearly all tropical and subtropical areas of the globe with some indication of their prevalence and their significance as public health problems. Dr. McKinley will have the thanks of all students of tropical disease. *A. G. Bagshawe.*

PATERSON (A. R.) [Director of Medical Services, Kenya Colony] with the Assistance of Many Officers of the Agricultural, Education, Forestry and Medical Departments of Kenya. **The Book of Civilization. Part II. The Story of the Forest and the Land and the Men and the Cattle.**—pp. vii+52. With 3 plates (2 coloured). 1935. London: New York: Toronto. Longmans, Green & Co. [1*s.*]

As the reviewer of Part I stated (this *Bulletin*, 1935, Vol. 32, p. 306) this book has been written for Africans with a view to affording them help in realizing the problems at issue in proper housing, hygiene, farming, stock-raising, etc. Part II deals with "The story of the forest and the land and the men and the cattle." What do we want—the means to Happiness—Food supplies—Cultivation of Crops and cattle—The use of money as a means of exchange—The power to buy—A reason for producing.

Much that is said in regard to the wasteful methods adopted by natives in agriculture, etc., and the necessity for the adoption of newer ways, is all to the point. The loss to a country by the indiscriminate destruction of forest and similar problems are well demonstrated.

But many, whether they be medical men, educationists or anthropologists, will disagree with the writer of the book over some of the main issues and over many details, as was pointed out by the reviewer of Part I.

It is suggested, for instance, that wheaten bread, tea, coffee and sugar should be staple articles in the diet of the native and that water-filters should be used—a very dangerous doctrine. It is suggested that the great aim for the native should be the gain of sufficient money to pay for the schooling of his children—a very debatable point.

It is suggested that trade with Japan should be encouraged—one fails to see the reason.

The story is told in a phraseology which is doubtless an attempt to copy the method of story-telling among natives, reminiscent in some ways of the Old Testament. Such a method doubtless appeals to the author, but since it is written in English it is a question whether it would not have been better to introduce the native to straightforward English prose and thereby have saved many pages of text.

It is not obvious either why some half dozen footnotes are given to explain some simple words—" bare=uncovered," " trampled=walked heavily upon "—when at the same time the text is full of English idioms.

H. S. Stannus.

Printed under the authority of His Majesty's Stationery Office
by the South Essex Recorders, Ltd., High Road, Ilford.

(87) Wt. P1/144 1875 3/36 S.E.R. Ltd. Gp. 353.